By performing an A1C test, health providers can measure a patient's average glycemia over the preceding 2–3 months (22) and, thus, assess treatment efficacy. A1C testing should be performed routinely in all patients with diabetes, first to document the degree of glycemic control at initial assessment and then as part of continuing care. Since the A1C test reflects mean glycemia over the preceding 2–3 months, measurement approximately every 3 months is required to determine whether a patient's metabolic control has been reached and maintained within the target range. Thus, regular performance of the A1C test permits detection of departures from the target (Table 6) in a timely fashion. For any individual patient, the frequency of A1C testing should be dependent on the clinical situation, the treatment regimen used, and the judgment of the clinician.

View this table: **Table 6— Summary of recommendations for adults with diabetes**
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The A1C test is subject to certain limitations. Conditions that affect erythrocyte turnover (hemolysis, blood loss) and hemoglobin variants must be considered, particularly when the A1C result does not correlate with the patient's clinical situation (22). The availability of the A1C result at the time that the patient is seen (point-of-care testing) has been reported to result in the frequency of intensification of therapy and improvement in glycemic control (23,24).

Glycemic control is best judged by the combination of the results of the patient's SMBG testing (as performed) and the current A1C result. The A1C should be used not only to assess the patient's control over the preceding 2–3 months, but also as a check on the accuracy of the meter (or the patient's self-reported results) and the adequacy of the SMBG testing schedule. Table 7 contains the correlation between A1C levels and mean plasma glucose levels based on data from the Diabetes Control and Complications Trial (DCCT) (25).

View this table: **Table 7— Correlation between A1C level and mean plasma glucose levels on multiple testing over 2–3 months (25)**
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2. Glycemic goals

Recommendations

- Lowering A1C has been associated with a reduction of microvascular and neuropathic complications of diabetes (A) and possibly macrovascular disease (B).
- The A1C goal *for patients in general* is an A1C goal of <7%. (B)

- The A1C goal *for the individual patient* is an A1C as close to normal (<6%) as possible without significant hypoglycemia. (E)
- Less stringent treatment goals may be appropriate for patients with a history of severe hypoglycemia, patients with limited life expectancies, very young children or older adults, and individuals with comorbid conditions. (E)
- Aggressive glycemic management with insulin may reduce morbidity in patients with severe acute illness, perioperatively, following myocardial infarction, and in pregnancy. (B)

Glycemic control is fundamental to the management of diabetes. The goal of therapy is to achieve an A1C as close to normal as possible (representing normal fasting and postprandial glucose concentrations) in the absence of hypoglycemia. However, this goal is difficult to achieve with present therapies (26). Prospective, randomized, clinical trials in type 1 diabetes such as the DCCT (27,28) have shown that improved glycemic control is associated with sustained decreased rates of microvascular (retinopathy and nephropathy), macrovascular, and neuropathic complications (28–31).

In type 2 diabetes, the U.K. Prospective Diabetes Study (UKPDS) demonstrated significant reductions in microvascular and neuropathic complications with intensive therapy (32–34). The potential of intensive glycemic control to reduce CVD in type 2 diabetes is supported by epidemiological studies (32–34) and a recent meta-analysis (35), but this potential benefit on CVD events has not been demonstrated in a randomized clinical trial.

In each of these large randomized prospective clinical trials, treatment regimens that reduced average A1C to ~7% (~1% above the upper limits of normal) were associated with fewer long-term microvascular complications; however, intensive control was found to increase the risk of severe hypoglycemia and weight gain (31,34).

Recommended glycemic goals for nonpregnant individuals are shown in Table 6. A major limitation to the available data is that they do not identify the optimum level of control for particular patients, as there are individual differences in the risks of hypoglycemia, weight gain, and other adverse effects. Furthermore, with multifactorial interventions, it is unclear how different components (e.g., educational interventions, glycemic targets, lifestyle changes, pharmacological agents) contribute to the reduction of complications. There are no clinical trial data available for the effects of glycemic control in patients with advanced complications, the elderly (≥65 years of age), or young children (<13 years of age). Less stringent treatment goals may be appropriate for patients with limited life expectancies, in the very young or older adults, and in individuals with comorbid conditions. Severe or frequent hypoglycemia is an indication for the modification of treatment regimens, including setting higher glycemic goals.

More stringent goals (i.e., a normal A1C, <6%) should be considered in individual patients based on epidemiological analyses suggesting that there is no lower limit of A1C at which further lowering does not reduce the risk of complications, at the risk of increased hypoglycemia (particularly in those with type 1 diabetes). However, the absolute risks and benefits of lower targets are unknown. The risks and benefits of an A1C goal of <6% are currently being tested in an ongoing study (ACCORD [Action to Control Cardiovascular Risk in Diabetes]) of type 2 diabetes.

Elevated postchallenge (2-h OGTT) glucose values have been associated with increased cardiovascular risk independent of FPG in some epidemiological studies. Postprandial plasma glucose (PPG) levels >140 mg/dl are unusual in nondiabetic individuals, although large evening meals can be followed by plasma glucose values up to 180 mg/dl. There are now pharmacological agents that primarily modify PPG and thereby reduce A1C in parallel. Thus, in individuals who have premeal glucose values within target but are not meeting A1C targets, monitoring PPG 1–2 h after the start of the meal and treatment aimed at reducing PPG values <180 mg/dl may lower A1C. However, it should be noted that the effect of these approaches on micro- or macrovascular complications has not been studied (36).

As regards goals for glycemic control for women with GDM, recommendations from the Fourth International Workshop-Conference on Gestational Diabetes suggest lowering maternal capillary blood glucose concentrations to ≤95 mg/dl (5.3 mmol/l) fasting, ≤140 mg/dl (7.8 mmol/l) at 1 h, and/or ≤120 mg/dl (6.7 mmol/l) at 2 h after the meal (37). For further information on GDM, refer to the ADA position statement (14). For information on glycemic control during pregnancy in women with preexisting diabetes, refer to ref. 38.

3. Approach to treatment.

A consensus statement from the ADA and the European Association for the Study of Diabetes on the approach to management of hyperglycemia in individuals with type 2 diabetes has recently been published (39). Early intervention with metformin in combination with lifestyle changes (MNT and exercise) with continuing, timely augmentation therapy with additional agents (including early initiation of insulin therapy) as a means of achieving and maintaining recommended levels of glycemic control (i.e., A1C <7% for most patients) are highlights of this approach. See Fig. 1 for metabolic management of type 2 diabetes.

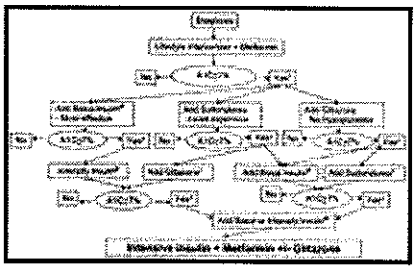

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Figure 1— Algorithm for the metabolic management of type 2 diabetes. Reinforce lifestyle intervention at every visit. *Check A1C every 3 months until <7% and then at least every 6 months. +Although three oral agents can be used, initiation and intensification of insulin therapy is preferred based on effectiveness and expense. #See Fig. 1 in ref. 39 for initiation and adjustment of insulin.

Early initiation of insulin would be a safer approach for individuals presenting with weight loss, more severe symptoms, and glucose values >250–300 mg/dl.

Insulin therapy, consisting of intermediate- or long-acting basal insulin in combination with premeal

rapid- or short-acting insulin is recommended for all patients with type 1 diabetes. An algorithm for adjusting premeal insulin doses to correct for blood glucose values outside of target ranges is appropriate for most patients with type 1 diabetes and insulin-treated type 2 diabetes. There are excellent reviews available that guide the initiation and management of insulin therapy to achieve desired glycemic goals (40,41).

D. MNT (42)

Recommendations

Diabetes and obesity management

- Individuals who have pre-diabetes or diabetes should receive individualized MNT as needed to achieve treatment goals, preferably provided by a registered dietitian familiar with the components of diabetes MNT. (B)
- MNT should be covered by insurance and other payors. (E)
- In overweight and obese insulin-resistant individuals, modest weight loss has been shown to reduce insulin resistance. Thus, weight loss is recommended for all overweight or obese individuals who have or are at risk for diabetes. (A)
- Structured programs that emphasize lifestyle changes, including education, reduced energy and fat (~30% of total energy) intake, regular physical activity, and regular participant contact, can produce long-term weight loss on the order of 5–7% of starting weight. Thus, lifestyle change should be the primary approach to weight loss. (A)
- Physical activity and behavior modification are important components of weight loss programs and are most helpful in maintenance of weight loss. (B)

Fat intake

- Saturated fat intake should be <7% of total calories. (A)
- Intake of *trans* fat should be minimized. (E)

Carbohydrate intake

- Monitoring carbohydrate, whether by carbohydrate counting, exchanges, or experience-based estimation, remains a key strategy in achieving glycemic control. (A)
- For individuals with diabetes, the use of the glycemic index and glycemic load may provide a

Case 1:05-cv-00360-SLR Document 401-10 Filed 05/13/2008 Page 5 of 50

modest additional benefit for glycemic control over that observed when total carbohydrate is considered alone. (B)
- There is not sufficient evidence to recommend use of glycemic index or glycemic load for prevention of diabetes, although foods high in fiber are encouraged. (E)
- Low-carbohydrate diets (restricting total carbohydrate to <130 g/day) are not recommended in the treatment of overweight/obesity. The long-term effects of these diets are unknown, and although such diets produce short-term weight loss, maintenance of weight loss is similar to that from low-fat diets and the impact on CVD risk profile is uncertain. (B)

Other nutrition recommendations

- Sugar alcohols and nonnutritive sweeteners are safe when consumed within the acceptable daily intake levels established by the Food and Drug Administration (FDA). (A)
- If adults with diabetes choose to use alcohol, daily intake should be limited to a moderate amount (one drink per day or less for adult women and two drinks per day or less for adult men). (E)
- Routine supplementation with antioxidants, such as vitamins E and C and carotene, is not advised because of lack of evidence of efficacy and concern related to long-term safety. (A)
- Benefit from chromium supplementation in people with diabetes or obesity has not been conclusively demonstrated and, therefore, cannot be recommended. (E)

MNT is an integral component of diabetes prevention, management, and self-management education. In addition to its role in preventing and controlling diabetes, ADA recognizes the importance of nutrition as an essential component of an overall healthy lifestyle. These recommendations are based on principles of good nutrition for the overall population from the 2005 Dietary Guidelines (43) and the recommended dietary allowances (RDAs) from the Institute of Medicine of the National Academies of Sciences (44). A review of the evidence regarding nutrition in preventing and controlling diabetes and its complications for the above nutrition recommendations and additional nutrition-related recommendations can be found elsewhere in this document. Achieving nutrition-related goals requires a coordinated team effort that includes the active involvement of the person with pre-diabetes or diabetes. Because of the complexity of nutrition issues, it is recommended that a registered dietitian who is knowledgeable and skilled in implementing nutrition therapy into diabetes management and education be the team member who provides MNT. However, it is essential that all team members are knowledgeable about nutrition therapy and are supportive of the person with diabetes.

For those individuals seeking guidance regarding macronutrient distribution, the DRIs may be helpful. The DRI report recommends that to meet the body's daily nutritional needs while minimizing risk for chronic diseases, adults (in general, not specifically those with diabetes) should consume 45–65% of total energy from carbohydrate, 20–35% from fat, and 10–35% from protein (44). The best mix of carbohydrate, protein, and fat appears to vary depending on individual circumstances.

▶ E. DSME

DJA-1403

Recommendations

- People with diabetes should receive DSME according to national standards when their diabetes is diagnosed and as needed thereafter. (B)
- DSME should be provided by health care providers who are qualified to provide that DSME based on their professional training and continuing education. (E)
- DSME should address psychosocial issues, since emotional well-being is strongly associated with positive diabetes outcomes. (C)
- DSME should be reimbursed by third-party payors. (E)

DSME is an essential element of diabetes care (45–51), and National Standards for DSME are based on evidence for its benefits. Education helps people with diabetes initiate effective self-care when they are first diagnosed. Ongoing DSME also helps people with diabetes maintain effective self-management as their diabetes presents new challenges and treatment advances become available. DSME helps patients optimize metabolic control, prevent and manage complications, and maximize quality of life, in a cost-effective manner.

Evidence for the benefits of DSME

Since the 1990s, there has been a shift from a didactic approach with DSME focusing on providing information to a skill-based approach that focuses on helping those with diabetes make informed self-management choices. Several studies have found that DSME is associated with improved diabetes knowledge (46), improved self-care behavior (46), improved clinical outcomes such as lower A1C (47,48,50,51), lower self-reported weight (46), and improved quality of life (49). Better outcomes were reported for DSME that were longer and included follow-up support (46), that were tailored to individual needs and preferences (45), and that addressed psychosocial issues (45,46,50).

The national standards for DSME

ADA-recognized DSME programs have staff that includes at least a registered nurse and a registered dietitian; these staff must be certified diabetes educators or have recent experience in diabetes education and management. The curriculum of ADA-recognized DSME programs must cover all areas of diabetes management, with the assessed needs of the individual determining which areas are addressed. All ADA-recognized DSME programs utilize a process of continuous quality improvement to evaluate the effectiveness of the DSME provided and to identify opportunities for improvement.

Reimbursement for DSME

DSME is reimbursed as part of the Medicare program as overseen by the Centers for Medicare and Medicaid Services (CMS) (www.cms.hhs.gov/DiabetesSelfManagement).

F. Physical activity

Recommendations

- To improve glycemic control, assist with weight maintenance, and reduce risk of CVD, at least 150 min/week of moderate-intensity aerobic physical activity (50–70% of maximum heart rate) and/or at least 90 min/week of vigorous aerobic exercise (>70% of maximum heart rate) is recommended. The physical activity should be distributed over at least 3 days/week and with no more than two 2 consecutive days without physical activity. (A)
- In the absence of contraindications, people with type 2 diabetes should be encouraged to perform resistance exercise three times a week, targeting all major muscle groups, progressing to three sets of 8–10 repetitions at a weight that cannot be lifted more than 8–10 times. (A)

Indications for graded exercise test with electrocardiogram monitoring

- A graded exercise test with electrocardiogram (ECG) monitoring should be seriously considered before undertaking aerobic physical activity with intensity exceeding the demands of everyday living (more intense than brisk walking) in previously sedentary diabetic individuals whose 10-year risk of a coronary event is likely to be ≥10%. (E)

ADA technical reviews on exercise in patients with diabetes have summarized the value of exercise in the diabetes management plan (52,53). Regular exercise has been shown to improve blood glucose control, reduce cardiovascular risk factors, contribute to weight loss, and improve well-being. Furthermore, regular exercise may prevent type 2 diabetes in high-risk individuals (8–10).

Definitions

The following definitions are based on those outlined in *Physical Activity and Health*, the 1996 report of the Surgeon General (54). Physical activity is defined as bodily movement produced by the contraction of skeletal muscle that requires energy expenditure in excess of resting energy expenditure. Exercise is a subset of physical activity: planned, structured, and repetitive bodily movement performed to improve or maintain one or more component of physical fitness. Aerobic exercise consists of rhythmic, repeated,

and continuous movements of the same large muscle groups for at least 10 min at a time. Examples include walking, bicycling, jogging, swimming, water aerobics, and many sports. Resistance exercise consists of activities that use muscular strength to move a weight or work against a resistive load. Examples include weight lifting and exercises using weight machines.

Effects of structured exercise interventions on glycemic control and body weight in type 2 diabetes
Boulé et al. (55) undertook a systematic review and meta-analysis on the effects of structured exercise interventions in clinical trials of duration ≥8 weeks on A1C and body mass in people with type 2 diabetes. Twelve aerobic training studies and two resistance training studies were included (totaling 504 subjects), and the results were pooled using standard meta-analytic statistical methods. Postintervention A1C was significantly lower in exercise than control groups. Metaregression confirmed that the beneficial effect of exercise on A1C was independent of any effect on body weight. Therefore, structured exercise programs had a statistically and clinically significant beneficial effect on glycemic control, and this effect was not mediated primarily by weight loss.

Boulé et al. (56) later undertook a meta-analysis of the interrelationships among exercise intensity, exercise volume, change in cardiorespiratory fitness, and change in A1C. This meta-analysis provides support for higher-intensity aerobic exercise in people with type 2 diabetes as a means of improving A1C. These results would provide support for encouraging type 2 diabetic individuals who are already exercising at moderate intensity to consider increasing the intensity of their exercise in order to obtain additional benefits in both aerobic fitness and glycemic control.

Frequency of exercise
The U.S. Surgeon General's report (54) recommended that most people accumulate ≥30 min of moderate-intensity activity on most, ideally all, days of the week. The American College of Sports Medicine now recommends including resistance training in fitness programs for adults with type 2 diabetes (57). Resistance exercise improves insulin sensitivity to about the same extent as aerobic exercise (58). Two clinical trials published in 2002 provided strong evidence for the value of resistance training in type 2 diabetes (59,60).

Evaluation of the diabetic patient before recommending an exercise program
Before beginning a program of physical activity more vigorous than brisk walking, people with diabetes should be assessed for conditions that might be associated with increased likelihood of CVD or that might contraindicate certain types of exercise or predispose to injury, such as uncontrolled hypertension, severe autonomic neuropathy, severe peripheral neuropathy, and preproliferative or proliferative retinopathy or macular edema. The patient's age and previous physical activity level should be considered.

A recent systematic review for the U.S. Preventive Services Task Force came to the conclusion that stress tests should usually not be recommended to detect ischemia in asymptomatic individuals at low CAD risk (<10% risk of a cardiac event over 10 years) because the risks of subsequent invasive testing triggered by false-positive tests outweighed the expected benefits from detection of previously unsuspected ischemia (61,62).

Case 1:05-cv-00300-SLR Document 401-10 Filed 05/13/2008 Page 5 of 30

Exercise in the presence of nonoptimal glycemic control

Hyperglycemia.

When people with type 1 diabetes are deprived of insulin for 12–48 h and are ketotic, exercise can worsen hyperglycemia and ketosis (63). Vigorous activity should probably be avoided in the presence of ketosis. However, provided the patient feels well and urine and/or blood ketones are negative, it is not necessary to postpone exercise based simply on hyperglycemia.

Hypoglycemia.

In individuals taking insulin and/or insulin secretagogues, physical activity can cause hypoglycemia if medication dose or carbohydrate consumption is not altered. Hypoglycemia is rare in diabetic individuals who are not treated with insulin or insulin secretagogues. Added carbohydrate should be ingested if preexercise glucose levels are <100 mg/dl (5.6 mmol/l) (64). Supplementary carbohydrate is generally not necessary for individuals treated only with diet, metformin, α-glucosidase inhibitors, and/or TZDs without insulin or a secretagogue (65).

Exercise in the presence of specific long-term complications of diabetes

Retinopathy.

In the presence of proliferative diabetic retinopathy (PDR) or severe non-PDR (NPDR), vigorous aerobic or resistance exercise may be contraindicated because of the risk of triggering vitreous hemorrhage or retinal detachment (66).

Peripheral neuropathy.

Decreased pain sensation in the extremities results in increased risk of skin breakdown and infection and of Charcot joint destruction. Therefore, in the presence of severe peripheral neuropathy, it may be best to encourage non–weight-bearing activities such as swimming, bicycling, or arm exercises (67,68).

Autonomic neuropathy.

Autonomic neuropathy can increase the risk of exercise-induced injury by decreasing cardiac responsiveness to exercise, postural hypotension, impaired thermoregulation due to impaired skin blood flow and sweating, impaired night vision due to impaired papillary reaction, impaired thirst increasing risk of dehydration, and gastroparesis with unpredictable food delivery (67). Autonomic neuropathy is also strongly associated with CVD in people with diabetes (69,70). People with diabetic autonomic neuropathy should definitely undergo cardiac investigation before beginning physical activity more intense than that to which they are accustomed.

Microalbuminuria and nephropathy.

Physical activity can acutely increase urinary protein excretion. There is no evidence from clinical trials or cohort studies demonstrating that vigorous exercise increases the rate of progression of diabetic kidney disease. There may be no need for any specific exercise restrictions for people with diabetic kidney disease (71).

G. Psychosocial assessment and care

Recommendations

▲ TOP
▲ INTRODUCTION

- Preliminary assessment of psychological and social status should be included as part of the medical management of diabetes. (E)
- Psychosocial screening should include but is not limited to attitudes about the illness, expectations for medical management and outcomes, affect/mood, general and diabetes-related quality of life, resources (financial, social, and emotional), and psychiatric history. (E)
- Screening for psychosocial problems such as depression, eating disorders, and cognitive impairment is needed when adherence to the medical regimen is poor. (E)
- It is preferable to incorporate psychological treatment into routine care rather than wait for identification of a specific problem or deterioration in psychological status. (E)

Psychological and social state can impact the patient's ability to carry out diabetes care tasks (72–77). As a result, health status may be compromised. Family conflict around diabetes care tasks is also common and may interfere with treatment outcomes (78). There are opportunities for the clinician to assess psychosocial status in a timely and efficient manner so that referral for appropriate services can be accomplished (79).

Key opportunities for screening of psychosocial status occur at diagnosis, during regularly scheduled management visits, during hospitalizations, at discovery of complications, or at the discretion of the clinician when problems in glucose control, quality of life, or adherence are identified (80). Patients are likely to exhibit psychological vulnerability at diagnosis and when their medical status changes, i.e., the end of the honeymoon period, when the need for intensified treatment is evident, and when complications are discovered (75,77).

Psychosocial screening should include but is not limited to attitudes about the illness, expectations for medical management and outcomes, affect/mood, general and diabetes-related quality of life, resources (financial, social, and emotional) (76), and psychiatric history (77,80,81). Particular attention needs to be paid to gross noncompliance with medical regimen (due to self or others) (81), depression with the possibility of self-harm (73,74), indications of an eating disorder (82) or a problem that appears to be organic in origin, and cognitive functioning that significantly impairs judgment (74). In these cases, immediate referral for further evaluation by a mental health specialist familiar with diabetes management should occur. Behavioral assessment of management skills is also recommended.

It is preferable to incorporate psychological treatment into routine care rather than waiting for

identification of a specific problem or deterioration in psychological status (79). Screening tools can facilitate this goal, and although the clinician may not feel qualified to treat psychological problems, utilizing the patient-provider relationship as a foundation for further treatment can increase the likelihood that the patient will accept referral for other services. It is important to establish that emotional well-being is part of diabetes management (80).

H. Referral for diabetes management

For a variety of reasons, some people with diabetes and their health care providers do not achieve the desired goals of treatment (Table 6). Intensification of the treatment regimen is suggested and includes identification (or assessment) of barriers to adherence, culturally appropriate and enhanced DSME, comanagement with a diabetes team, change in pharmacological therapy, initiation of or increase in SMBG, more frequent contact with the patient, and referral to an endocrinologist.

I. Intercurrent illness

The stress of illness, trauma, and/or surgery frequently aggravates glycemic control and may precipitate diabetic ketoacidosis (DKA) or nonketotic hyperosmolar state. Any condition leading to deterioration in glycemic control necessitates more frequent monitoring of blood glucose and urine or blood ketones. A vomiting illness accompanied by ketosis may indicate DKA, a life-threatening condition that requires immediate medical care to prevent complications and death; the possibility of DKA should always be considered (83). Marked hyperglycemia requires temporary adjustment of the

treatment program and, if accompanied by ketosis, frequent interaction with the diabetes care team. The patient treated with oral glucose-lowering agents or MNT alone may temporarily require insulin. Adequate fluid and caloric intake must be assured. Infection or dehydration is more likely to necessitate hospitalization of the person with diabetes than the person without diabetes. The hospitalized patient should be treated by a physician with expertise in the management of diabetes, and recent studies suggest that achieving very stringent glycemic control may reduce mortality in the immediate postmyocardial infarction period (84). Aggressive glycemic management with insulin may reduce morbidity in patients with severe acute illness (85).

For further information on management of patients in the hospital with DKA or nonketotic hyperosmolar state, refer to the ADA position statement (83).

J. Hypoglycemia

Recommendations

- Glucose (15–20 g) is the preferred treatment for hypoglycemia, although any form of carbohydrate that contains glucose may be used, and treatment effects should be apparent in 15 min. (A)
- Treatment effects on hypoglycemia may only be temporarily corrected. Therefore, plasma glucose should be retested in ~15 min, as additional treatment may be necessary. (B)
- Glucagon should be prescribed for all patients at significant risk of severe hypoglycemia and does not require a health care professional for its administration. (E)

Hypoglycemia, especially in insulin-treated patients, is the leading limiting factor in the glycemic management of type 1 and type 2 diabetes (86). Treatment of hypoglycemia (plasma glucose <70 mg/dl) requires ingestion of glucose- or carbohydrate-containing foods. The acute glycemic response correlates better with the glucose content than with the carbohydrate content of the food. Although pure glucose may be the preferred treatment, any form of carbohydrate that contains glucose will raise blood

Case 1:05-cv-00360-SLR Document 401-10 Filed 05/13/2008 Page 13 of 30

glucose. Adding protein to carbohydrate does not affect the glycemic response and does not prevent subsequent hypoglycemia. Adding fat, however, may retard and then prolong the acute glycemic response (87).

Rare situations of severe hypoglycemia (where the individual requires the assistance of another person and cannot be treated with oral carbohydrate) should be treated using emergency glucagon kits, which require a prescription. Those in close contact with, or having custodial care of, people with diabetes, such as family members, roommates, school personnel, child care providers, correctional institution staff, and coworkers, should be instructed in use of such kits. An individual does not need to be a health care professional to safely administer glucagon. Care should be taken to ensure that unexpired glucagon kits are available.

K. Immunization

Recommendations

- Annually provide an influenza vaccine to all diabetic patients ≥6 months of age. (C)
- Provide at least one lifetime pneumococcal vaccine for adults with diabetes. A one-time revaccination is recommended for individuals >64 years of age previously immunized when they were <65 years of age if the vaccine was administered >5 years ago. Other indications for repeat vaccination include nephrotic syndrome, chronic renal disease, and other immunocompromised states, such as after transplantation. (C)

Influenza and pneumonia are common, preventable infectious diseases associated with high mortality and morbidity in the elderly and in people with chronic diseases. There are limited studies reporting the morbidity and mortality of influenza and pneumococcal pneumonia specifically in people with diabetes. Observational studies of patients with a variety of chronic illnesses, including diabetes, show that these conditions are associated with an increase in hospitalizations for influenza and its complications. Based on a case-control series, influenza vaccine has been shown to reduce diabetes-related hospital admission by as much as 79% during flu epidemics (88). People with diabetes may be at increased risk of the bacteremic form of pneumococcal infection and have been reported to have a high risk of nosocomial bacteremia, which has a mortality rate as high as 50%.

DJA-1411

Case 1:05-cv-00360-SLR Document 401-10 Filed 05/13/2008 Page 14 of 50

Safe and effective vaccines are available that can greatly reduce the risk of serious complications from these diseases (88,89). There is sufficient evidence to support that people with diabetes have appropriate serologic and clinical responses to these vaccinations. The Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices recommends influenza and pneumococcal vaccines for all individuals >65 years of age, as well as for all individuals of any age with diabetes.

For a complete discussion on the prevention of influenza and pneumococcal disease in people with diabetes, consult the technical review and position statement on this subject (90,91).

VI. PREVENTION AND MANAGEMENT OF DIABETES COMPLICATIONS

A. CVD

CVD is the major cause of mortality for individuals with diabetes. It is also a major contributor to morbidity and direct and indirect costs of diabetes. Type 2 diabetes is an independent risk factor for macrovascular disease, and its common coexisting conditions (e.g., hypertension and dyslipidemia) are also risk factors.

Studies have shown the efficacy of reducing cardiovascular risk factors in preventing or slowing CVD. Evidence is summarized in the following sections and reviewed in detail in the ADA technical reviews on hypertension (92), dyslipidemia (93), aspirin therapy (131), and smoking cessation (94) and the consensus statement on CHD in people with diabetes (95). Emphasis should be placed on reducing cardiovascular risk factors, when possible, and clinicians should be alert for signs and symptoms of atherosclerosis.

1. Hypertension/blood pressure control

Recommendations

Screening and diagnosis

- Blood pressure should be measured at every routine diabetes visit. Patients found to have systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg should have blood pressure confirmed on a separate day. (C)

Goals

DJA-1412

- Patients with diabetes should be treated to a systolic blood pressure <130 mmHg. (C)
- Patients with diabetes should be treated to a diastolic blood pressure <80 mmHg. (B)

Treatment

- Patients with hypertension (systolic blood pressure ≥140 or diastolic blood pressure ≥90 mmHg) should receive drug therapy in addition to lifestyle and behavioral therapy. (A)
- Multiple drug therapy (two or more agents at proper doses) is generally required to achieve blood pressure targets. (B)
- Patients with a systolic blood pressure of 130–139 mmHg or a diastolic blood pressure of 80–89 mmHg should be given lifestyle and behavioral therapy alone for a maximum of 3 months and then, if targets are not achieved, in addition, be treated with pharmacological agents that block the renin-angiotensin system. (E)
- Initial drug therapy for those with a blood pressure >140/90 mmHg should be with a drug class demonstrated to reduce CVD events in patients with diabetes (ACE inhibitors, angiotensin receptor blockers [ARBs], ß-blockers, diuretics, and calcium channel blockers). (A)
- All patients with diabetes and hypertension should be treated with a regimen that includes either an ACE inhibitor or an ARB. If one class is not tolerated, the other should be substituted. If needed to achieve blood pressure targets, a thiazide diuretic should be added. (E)
- If ACE inhibitors, ARBs, or diuretics are used, monitor renal function and serum potassium levels. (E)
    - In patients with type 1 diabetes, with hypertension and any degree of albuminuria, ACE inhibitors have been shown to delay the progression of nephropathy. (A)
    - In patients with type 2 diabetes, hypertension, and microalbuminuria, ACE inhibitors and ARBs have been shown to delay the progression to macroalbuminuria. (A)
    - In those with type 2 diabetes, hypertension, macroalbuminuria, and renal insufficiency, ARBs have been shown to delay the progression of nephropathy. (A)

- In pregnant patients with diabetes and chronic hypertension, blood pressure target goals of 110–129/65–79 mmHg are suggested in the interest of long-term maternal health and minimizing impaired fetal growth. ACE inhibitors and ARBs are contraindicated during pregnancy. (E)
- In elderly hypertensive patients, blood pressure should be lowered gradually to avoid complications. (E)
- Patients not achieving target blood pressure despite multiple drug therapy should be referred to a physician experienced in the care of patients with hypertension. (E)
- Orthostatic measurement of blood pressure should be performed in people with diabetes and hypertension when clinically indicated. (E)

Hypertension (blood pressure ≥140/90 mmHg) is a common comorbidity of diabetes, affecting the majority of people with diabetes, depending on type of diabetes, age, obesity, and ethnicity. Hypertension is also a major risk factor for CVD and microvascular complications such as retinopathy and nephropathy. In type 1 diabetes, hypertension is often the result of underlying nephropathy. In type 2 diabetes, hypertension may be present as part of the metabolic syndrome (i.e., obesity, hyperglycemia,

and dyslipidemia), which is accompanied by high rates of CVD.

Randomized clinical trials have demonstrated the benefit (reduction of CHD events, stroke, and nephropathy) of lowering blood pressure to <140 mmHg systolic and <80 mmHg diastolic in individuals with diabetes (96–99). Epidemiologic analyses show that blood pressure >115/75 mmHg are associated with increased cardiovascular event rates and mortality in individuals with diabetes (96,100,101). Therefore, a target blood pressure goal of <130/80 mmHg is reasonable if it can be safely achieved.

Although there are no well-controlled studies of diet and exercise in the treatment of hypertension in individuals with diabetes, reducing sodium intake and body weight (when indicated); increasing consumption of fruits, vegetables, and low-fat dairy products; avoiding excessive alcohol consumption; and increasing activity levels have been shown to be effective in reducing blood pressure in nondiabetic individuals (102). These nonpharmacological strategies may also positively affect glycemia and lipid control. Their effects on cardiovascular events have not been well measured.

Lowering of blood pressure with regimens based on antihypertensive drugs, including ACE inhibitors, ARBs, ß-blockers, diuretics, and calcium channel blockers, has been shown to be effective in lowering cardiovascular events. Several studies suggest that ACE inhibitors may be superior to dihydropyridine calcium channel blockers (DCCBs) in reducing cardiovascular events (103,104). Additionally, in people with diabetic nephropathy, ARBs may be superior to DCCBs for reducing heart failure but not overall cardiovascular events (105). Conversely, in the recently completed INVEST (International Verapamil-Trandolapril Study) of >22,000 people with CAD and hypertension, the non-DCCB verapamil demonstrated a similar reduction in cardiovascular mortality to a ß-blocker. Moreover, this relationship held true in the diabetic subgroup (106).

ACE inhibitors have been shown to improve cardiovascular outcomes in high–cardiovascular risk patients with or without hypertension (107,108). In patients with congestive heart failure (CHF), the addition of ARBs to either ACE inhibitors or other therapies reduces the risk of cardiovascular death or hospitalization for heart failure (109–111). In one study, an ARB was superior to a ß-blocker as a therapy to improve cardiovascular outcomes in a subset of diabetic patients with hypertension and left ventricular hypertrophy (112). The compelling effect of ACE inhibitors or ARBs in patients with albuminuria or renal insufficiency provides additional rationale for use of these agents (see section VI, B below).

The ALLHAT (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial), a large randomized trial of different initial blood pressure pharmacological therapies, found no large differences in initial therapy with chlorthalidone, amlodipine, or lisinopril. Diuretics appeared slightly more effective than other agents, particularly for reducing heart failure (113). The α-blocker arm of the ALLHAT was terminated after interim analysis showed that doxazosin was substantially less effective in reducing CHF than diuretic therapy (114).

Before beginning treatment, patients with elevated blood pressure should have their blood pressure reexamined within 1 month to confirm the presence of hypertension. Systolic blood pressure ≥160

mmHg or diastolic blood pressure ≥100 mmHg, however, mandates that immediate pharmacological therapy be initiated. Patients with hypertension should be seen as often as needed until the recommended blood pressure goal is obtained and then seen as necessary (96). In these patients, other cardiovascular risk factors, including obesity, hyperlipidemia, smoking, presence of microalbuminuria (assessed before initiation of treatment), and glycemic control, should be carefully assessed and treated. Many patients will require three or more drugs to reach target goals.

During pregnancy in diabetic women with chronic hypertension, target blood pressure goals of systolic blood pressure 110–129 mmHg and diastolic blood pressure 65–79 mmHg are reasonable, as they may contribute to long-term maternal health. Lower blood pressure levels may be associated with impaired fetal growth. During pregnancy, treatment with ACE inhibitors and ARBs is contraindicated, since they are likely to cause fetal damage. Antihypertensive drugs known to be effective and safe in pregnancy include methyldopa, labetalol, diltiazem, clonidine, and prazosin. Chronic diuretic use during pregnancy has been associated with restricted maternal plasma volume, which might reduce uteroplacental perfusion.

2. Dyslipidemia/lipid management

Recommendations
Screening

- In adult patients, test for lipid disorders at least annually and more often if needed to achieve goals. In adults with low-risk lipid values (LDL <100 mg/dl, HDL >50 mg/dl, and triglycerides <150 mg/dl), lipid assessments may be repeated every 2 years. (E)

Treatment recommendations and goals

- Lifestyle modification focusing on the reduction of saturated fat, *trans* fat, and cholesterol intake; weight loss (if indicated); and increased physical activity has been shown to improve the lipid profile in patients with diabetes. (A)
- In individuals without overt CVD
  - The primary goal is an LDL <100 mg/dl (2.6 mmol/l). (A)
  - For those over the age of 40 years, statin therapy to achieve an LDL reduction of 30–40% regardless of baseline LDL levels is recommended. (A)
  - For those under the age of 40 years but at increased risk due to other cardiovascular risk factors who do not achieve lipid goals with lifestyle modifications alone, the addition of pharmacological therapy is appropriate. (C)

- In individuals with overt CVD
  - All patients should be treated with a statin to achieve an LDL reduction of 30–40%. (A)
  - A lower LDL cholesterol goal of <70 mg/dl (1.8 mmol/l), using a high dose of a statin, is an option. (B)

- Lower triglycerides to <150 mg/dl (1.7 mmol/l) and raise HDL cholesterol to >40 mg/dl (1.0

mmol/l). In women, an HDL goal 10 mg/dl higher (>50 mg/dl) should be considered. (C)
- Lowering triglycerides and increasing HDL cholesterol with a fibrate is associated with a reduction in cardiovascular events in patients with clinical CVD, low HDL, and near-normal levels of LDL. (A)
- Combination therapy using statins and other lipid-lowering agents may be necessary to achieve lipid targets but has not been evaluated in outcomes studies for either CVD event reduction or safety. (E)
- Statin therapy is contraindicated in pregnancy. (E)

Patients with type 2 diabetes have an increased prevalence of lipid abnormalities, which contributes to higher rates of CVD. Lipid management aimed at lowering LDL cholesterol, raising HDL cholesterol, and lowering triglycerides has been shown to reduce macrovascular disease and mortality in patients with type 2 diabetes, particularly in those who have had prior cardiovascular events. In studies using HMG (hydroxymethylglutaryl)-CoA reductase inhibitors (statins), patients with diabetes achieved significant reductions in coronary and cerebrovascular events (115–118). In two studies using the fibric acid derivative gemfibrozil, reductions in cardiovascular end points were also achieved (119,120).

Target lipid levels are shown in Table 6. Lifestyle intervention, including MNT, increased physical activity, weight loss, and smoking cessation, should allow some patients to reach these lipid levels. Nutrition intervention should be tailored according to each patient's age, type of diabetes, pharmacological treatment, lipid levels, and other medical conditions and should focus on the reduction of saturated fat, cholesterol, and *trans* unsaturated fat intake. Glycemic control can also beneficially modify plasma lipid levels. Particularly in patients with very high triglycerides and poor glycemic control, glucose lowering may be necessary to control hypertriglyceridemia. Pharmacological treatment is indicated if there is an inadequate response to lifestyle modifications and improved glucose control. However, in patients with clinical CVD and LDL >100 mg/dl, pharmacological therapy should be initiated at the same time that lifestyle intervention is started. In patients with diabetes aged <40 years, similar consideration for LDL-lowering therapy should be given if they have increased cardiovascular risk (e.g., additional cardiovascular risk factors or long duration of diabetes). Very little clinical trial data exist for patients in this age-group.

The first priority of pharmacological therapy is to lower LDL cholesterol to a target goal of <100 mg/dl (2.60 mmol/l) or therapy to achieve a reduction in LDL of 30–40%. For LDL lowering, statins are the drugs of choice. Other drugs that lower LDL include nicotinic acid, ezetimbe, bile acid sequestrants, and fenofibrate (121,122).

The Heart Protection Study (118) demonstrated that in individuals with diabetes over the age of 40 years with a total cholesterol >135 mg/dl, LDL reduction of ~30% from baseline with the statin simvastatin was associated with an ~25% reduction in the first event rate for major coronary artery events independent of baseline LDL, preexisting vascular disease, type or duration of diabetes, or adequacy of glycemic control. Similarly, in the CARDS (Coronary Artery Diabetes Study) (124), patients with type 2 diabetes randomized to 10 mg atorvastatin daily had a significant reduction in cardiovascular events

including stroke.

Recent clinical trials in high-risk patients, such as those with acute coronary syndromes or previous cardiovascular events (125–127), have demonstrated that more aggressive therapy with high doses of statins to achieve an LDL of <70 mg/dl led to a significant reduction in further events. The risk of side effects with high doses of statins is significantly outweighed by the benefits of such therapy in these high-risk patients. Therefore, a reduction in LDL to a goal of <70 mg/dl is an option in very-high-risk patients with overt CVD (122). The combination of statins with other lipid-lowering drugs such as ezetimibe may allow achievement of the LDL goal with a lower dose of a statin in such patients (128), but no data are available as to whether such combination therapy is more effective than a statin alone in preventing cardiovascular events.

Relatively little data are available on lipid-lowering therapy in subjects with type 1 diabetes. In the Heart Protection Study, ~600 patients with type 1 diabetes had a proportionately similar, but not statistically significant, reduction in risk compared with patients with type 2 diabetes. Although the data are not definitive, consideration should be given for similar lipid-lowering therapy in type 1 diabetic patients as in type 2 diabetic patients, particularly if they have other cardiovascular risk factors or features of the metabolic syndrome.

If the HDL is <40 mg/dl and the LDL between 100 and 129 mg/dl, a fibric acid derivative or niacin might be used. Niacin is the most effective drug for raising HDL but can significantly increase blood glucose at high doses. More recent studies demonstrate that at modest doses (750–2,000 mg/day), significant benefits to LDL, HDL, and triglyceride levels are accompanied by only modest changes in glucose that are generally amenable to adjustment of diabetes therapy (129,130).

Combination therapy, with a statin and a fibrate or statin and niacin, may be efficacious for patients needing treatment for all three lipid fractions, but this combination is associated with an increased risk for abnormal transaminase levels, myositis, or rhabdomyolysis. The risk of rhabdomyolysis seems to be lower when statins are combined with fenofibrate than gemfibrozil. There is also a risk of a rise in plasma creatinine, particularly with fenofibrate. It is important to note that clinical trials with fibrates and niacin have demonstrated benefits in patients who were not being treated with statins and that there are no data available on reduction of events with such combinations. The risks may be greater in patients who are treated with combinations of these drugs with high doses of statins.

3. Antiplatelet agents

Recommendations

- Use aspirin therapy (75–162 mg/day) as a secondary prevention strategy in those with diabetes with a history of CVD. (A)
- Use aspirin therapy (75–162 mg/day) as a primary prevention strategy in those with:
    - Type 2 diabetes at increased cardiovascular risk, including those who are >40 years of age or who have additional risk factors (family history of CVD, hypertension, smoking,

Case 1:05-cv-00360-SLR Document 401-10 Filed 05/13/2008 Page 20 of 50

dyslipidemia, or albuminuria). (A)
- Type 1 diabetes at increased cardiovascular risk, including those who are >40 years of age or who have additional risk factors (family history of CVD, hypertension, smoking, dyslipidemia, or albuminuria). (C)

- Consider aspirin therapy in people between the age of 30 and 40 years, particularly in the presence of other cardiovascular risk factors. (E)
- Aspirin therapy should not be recommended for patients under the age of 21 years because of the increased risk of Reye's syndrome associated with aspirin use in this population. People <30 years have not been studied. (E)
- Combination therapy using other antiplatelet agents such as clopidrogel in addition to aspirin should be used in patients with severe and progressive CVD. (C)
- Other antiplatelet agents may be a reasonable alternative for high-risk patients with aspirin allergy, with bleeding tendency, who are receiving anticoagulant therapy, with recent gastrointestinal bleeding, and with clinically active hepatic disease who are not candidates for aspirin therapy. (E)

The use of aspirin in diabetes is reviewed in detail in the ADA technical review (131) and position statement (132) on aspirin therapy. Aspirin has been recommended as a primary (133,134) and secondary therapy to prevent cardiovascular events in diabetic and nondiabetic individuals. One large meta-analysis and several clinical trials demonstrate the efficacy of using aspirin as a preventive measure for cardiovascular events, including stroke and myocardial infarction. Many trials have shown an ~30% decrease in myocardial infarction and a 20% decrease in stroke in a wide range of patients, including young and middle-aged patients, patients with and without a history of CVD, males and females, and patients with hypertension.

Dosages used in most clinical trials ranged from 75 to 325 mg/day. There is no evidence to support any specific dose, but using the lowest possible dosage may help reduce side effects. There is no evidence for a specific age at which to start aspirin, but at ages <30 years, aspirin has not been studied.

Clopidogrel has been demonstrated to reduce CVD rates in diabetic individuals (135). Adjunctive therapy in very-high-risk patients or as alternative therapy in aspirin-intolerant patients should be considered.

4. Smoking cessation

Recommendations

- Advise all patients not to smoke. (A)
- Include smoking cessation counseling and other forms of treatment as a routine component of diabetes care. (B)

Issues of smoking in diabetes are reviewed in detail in the ADA technical review (94) and position

DJA-1418

statement (136) on smoking cessation. A large body of evidence from epidemiological, case-control, and cohort studies provides convincing documentation of the causal link between cigarette smoking and health risks. Cigarette smoking contributes to one of every five deaths in the U.S. and is the most important modifiable cause of premature death. Much of the prior work documenting the impact of smoking on health did not separately discuss results on subsets of individuals with diabetes, suggesting that the identified risks are at least equivalent to those found in the general population. Other studies of individuals with diabetes consistently found a heightened risk of morbidity and premature death associated with the development of macrovascular complications among smokers. Smoking is also related to the premature development of microvascular complications of diabetes and may have a role in the development of type 2 diabetes.

A number of large randomized clinical trials have demonstrated the efficacy and cost-effectiveness of counseling in changing smoking behavior. Such studies, combined with others specific to individuals with diabetes, suggest that smoking cessation counseling is effective in reducing tobacco use (137,138).

The routine and thorough assessment of tobacco use is important as a means of preventing smoking or encouraging cessation. Special considerations should include assessment of level of nicotine dependence, which is associated with difficulty in quitting and relapse.

5. CHD screening and treatment

Recommendations

- In patients >55 years of age, with or without hypertension but with another cardiovascular risk factor (history of CVD, dyslipidemia, microalbuminuria, or smoking), an ACE inhibitor (if not contraindicated) should be considered to reduce the risk of cardiovascular events. (A)
- In patients with a prior myocardial infarction or in patients undergoing major surgery, ß-blockers, in addition, should be considered to reduce mortality. (A)
- In asymptomatic patients, consider a risk factor evaluation to stratify patients by 10-year risk and treat risk factors accordingly. (B)
- In patients with treated CHF, metformin use is contraindicated. TZDs are associated with fluid retention, and their use can be complicated by the development of CHF. Caution in prescribing TZDs in the setting of known CHF or other heart diseases, as well as in patients with preexisting edema or concurrent insulin therapy, is required. (C)

CHD screening and treatment are reviewed in detail in the ADA consensus statement on CHD in people with diabetes (95). To identify the presence of CHD in diabetic patients without clear or suggestive symptoms of CAD, a risk factor–based approach to the initial diagnostic evaluation and subsequent follow-up is recommended. However, a recent study concluded that using current guidelines fails to detect a significant percentage of patients with silent ischemia (69).

At least annually, cardiovascular risk factors should be assessed. These risk factors include dyslipidemia, hypertension, smoking, a positive family history of premature coronary disease, and the

presence of micro- or macroalbuminuria. Abnormal risk factors should be treated as described elsewhere in these guidelines. Patients at increased CHD risk should receive aspirin and may warrant an ACE inhibitor.

Candidates for a diagnostic cardiac stress test include those with *1*) typical or atypical cardiac symptoms and *2*) an abnormal resting ECG. The screening of asymptomatic patients remains controversial.

Studies have demonstrated that a significant percentage of patients with diabetes who have no symptoms of CAD have abnormal stress tests, either by ECG or echo and nuclear perfusion imaging. Some of these patients, though clearly not all, have significant coronary stenoses if they proceed to angiography. It has also been demonstrated that patients with silent myocardial ischemia have a poorer prognosis than those with normal stress tests. Their risk is further accentuated if cardiac autonomic neuropathy coexists. Candidates for a screening cardiac stress test include those with *1*) a history of peripheral or carotid occlusive disease and *2*) sedentary lifestyle, age >35 years, and plans to begin a vigorous exercise program. There are no data to suggest that patients who start to increase their physical activity by walking or similar exercise increase their risk of a CVD event and therefore are unlikely to need a stress test.

It has previously been proposed to screen those with two or more additional cardiac risk factors. However, this likely includes the vast majority of patients with type 2 diabetes (given that the risk factors frequently cluster). The DIAD (Detection of Silent Myocardial Ischemia in Asymptomatic Diabetic Subjects) study suggested that conventional cardiac risk factors did not help to identify those patients with abnormal perfusion imaging (69).

Current evidence suggests that noninvasive tests can improve assessment of future CHD risk. There is, however, no current evidence that such testing in asymptomatic patients with risk factors improves outcomes or leads to better utilization of treatments (62).

Approximately 1 in 5 will have an abnormal test, and ~1 in 15 will have a major abnormality. More information is needed concerning prognosis, and the value of early intervention (invasive or noninvasive) before widespread screening is recommended. All patients irrespective of their CAD status should have aggressive risk factor modification, including control of glucose, lipids, and blood pressure and prophylactic aspirin therapy.

Patients with abnormal exercise ECG and patients unable to perform an exercise ECG require additional or alternative testing. Currently, stress nuclear perfusion and stress echocardiography are valuable next-level diagnostic procedures. A consultation with a cardiologist is recommended regarding further work-up.

When identified, the optimal therapeutic approach to the diabetic patient with silent myocardial ischemia is unknown. Certainly if major CAD is identified, aggressive intervention appears warranted. If minor stenoses are detected, however, it is unknown whether there is any benefit to further invasive evaluation and/or therapy. There are no well-conducted prospective trials with adequate control groups

to shed light on this subject. Accordingly, there are no evidence-based guidelines for screening the asymptomatic diabetic patient for CAD.

B. Nephropathy screening and treatment

Recommendations

General recommendations

- To reduce the risk and/or slow the progression of nephropathy, optimize glucose control. (A)
- To reduce the risk and/or slow the progression of nephropathy, optimize blood pressure control. (A)

Screening

- Perform an annual test for the presence of microalbuminuria in type 1 diabetic patients with diabetes duration of ≥5 years and in all type 2 diabetic patients, starting at diagnosis and during pregnancy. (E)
- Serum creatinine should be measured at least annually for the estimation of glomerular filtration rate (GFR) in all adults with diabetes regardless of the degree of urine albumin excretion. The serum creatinine alone should not be used as a measure of kidney function but instead used to estimate GFR and stage the level of chronic kidney disease (CKD). (E)

Treatment

- In the treatment of both micro- and macroalbuminuria, either ACE inhibitors or ARBs should be used except during pregnancy. (A)
- While there are no adequate head-to-head comparisons of ACE inhibitors and ARBs, there is clinical trial support for each of the following statements:
  - In patients with type 1 diabetes, with hypertension and any degree of albuminuria, ACE inhibitors have been shown to delay the progression of nephropathy. (A)
  - In patients with type 2 diabetes, hypertension, and microalbuminuria, ACE inhibitors and ARBs have been shown to delay the progression to macroalbuminuria. (A)
  - In patients with type 2 diabetes, hypertension, macroalbuminuria, and renal insufficiency (serum creatinine >1.5 mg/dl), ARBs have been shown to delay the progression of nephropathy. (A)
  - If one class is not tolerated, the other should be substituted. (E)

- Reduction of protein intake to 0.8–1.0 g · kg body wt^{-1} · day^{-1} in individuals with diabetes and the earlier stages of CKD and to 0.8 g · kg body wt^{-1} · day^{-1} in the later stages of CKD may improve measures of renal function (urine albumin excretion rate, GFR) and is recommended (B)
- To slow the progression of nephropathy, the use of DCCBs as initial therapy is not more effective than placebo. Their use in nephropathy should be restricted to additional therapy to further lower blood pressure in patients already treated with ACE inhibitors or ARBs. (B)
- In the setting of albuminuria or nephropathy, in patients unable to tolerate ACE inhibitors and/or ARBs, consider the use of non-DCCBs, ß-blockers, or diuretics for the management of blood pressure. Use of non-DCCBs may reduce albuminuria in diabetic patients, including during pregnancy. (E)
- If ACE inhibitors, ARBs, or diuretics are used, monitor serum potassium levels for the development of hyperkalemia. (B)
- Continued surveillance of microalbuminuria/proteinuria to assess both response to therapy and progression of disease is recommended. (E)
- Consider referral to a physician experienced in the care of diabetic renal disease when the estimated GFR has fallen to <60 ml/min per 1.73 m^2 or if difficulties occur in the management of hypertension or hyperkalemia. (B)

Diabetic nephropathy occurs in 20–40% of patients with diabetes and is the single leading cause of end-stage renal disease (ESRD). Persistent albuminuria in the range of 30–299 mg/24 h (microalbuminuria) has been shown to be the earliest stage of diabetic nephropathy in type 1 diabetes and a marker for development of nephropathy in type 2 diabetes. Microalbuminuria is also a well-established marker of increased CVD risk (139,140).

Patients with microalbuminuria who progress to macroalbuminuria (≥300 mg/24 h) are likely to progress to ESRD over a period of years (141,142). Over the past several years, a number of interventions have been demonstrated to reduce the risk and slow the progression of renal disease.

Intensive diabetes management with the goal of achieving near normoglycemia has been shown in large prospective randomized studies to delay the onset of microalbuminuria and the progression of micro- to macroalbuminuria in patients with type 1 (143,144) and type 2 (32,33) diabetes. The UKPDS provided strong evidence that control of blood pressure can reduce the development of nephropathy (97). In addition, large prospective randomized studies in patients with type 1 diabetes have demonstrated that achievement of lower levels of systolic blood pressure (<140 mmHg) resulting from treatment using ACE inhibitors provides a selective benefit over other antihypertensive drug classes in delaying the progression from micro- to macroalbuminuria and can slow the decline in GFR in patients with macroalbuminuria (145–147).

In addition, ACE inhibitors have been shown to reduce severe CVD (i.e., myocardial infarction, stroke, death), thus further supporting the use of these agents in patients with microalbuminuria (107). ARBs have also been shown to reduce the rate of progression from micro- to macroalbuminuria as well as ESRD in patients with type 2 diabetes (148–150). Some evidence suggests that ARBs have a smaller

magnitude of rise in potassium compared with ACE inhibitors in people with nephropathy (106). To slow the progression of nephropathy, the use of DCCBs as initial therapy is not more effective than placebo. Their use in nephropathy should be restricted to additional therapy to further lower blood pressure in patients already treated with ACE inhibitors or ARBs (105). In the setting of albuminuria or nephropathy, in patients unable to tolerate ACE inhibitors and/or ARBs, consider the use of non-DCCBs, ß-blockers, or diuretics for the management of blood pressure (106,151).

Studies in patients with varying stages of nephropathy have shown that protein restriction helps slow the progression of albuminuria, GFR decline, and occurrence of ESRD (152–154). Protein restriction should be considered particularly in patients whose nephropathy seems to be progressing despite optimal glucose and blood pressure control and use of ACE inhibitor and/or ARBs (155).

Screening for microalbuminuria can be performed by three methods: *1*) measurement of the albumin-to-creatinine ratio in a random spot collection (preferred method); *2*) 24-h collection with creatinine, allowing the simultaneous measurement of creatinine clearance; and *3*) timed (e.g., 4-h or overnight) collection.

The analysis of a spot sample for the albumin-to-creatinine ratio is strongly recommended by most authorities (156,157). The other two alternatives (24-h collection and a timed specimen) are rarely necessary. Measurement of a spot urine for albumin only, whether by immunoassay or by using a dipstick test specific for microalbumin, without simultaneously measuring urine creatinine, is less expensive than the recommended methods but is susceptible to false-negative and -positive determinations as a result of variation in urine concentration due to hydration and other factors.

At least two of three tests measured within a 6-month period should show elevated levels before a patient is designated as having microalbuminuria. Abnormalities of albumin excretion are defined in Table 8.

View this table: Table 8— Definitions of abnormalities in albumin excretion
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Screening for microalbuminuria is indicated in pregnancies complicated by diabetes, since microalbuminuria in the absence of urinary tract infection is a strong predictor of superimposed preeclampsia. In the presence of macroalbuminuria or urine dipstick proteinuria, estimation of GFR by serum creatinine (see below) or 24-h urine creatinine clearance is indicated to stage the patient's renal disease, and other tests may be necessary to diagnose preeclampsia.

Information on presence of urine albumin excretion in addition to level of GFR may be used to stage CKD according to the National Kidney Foundation. The current National Kidney Foundation classification (Table 9) is primarily based on GFR levels and therefore differs from some earlier staging

Case 1:05-cv-00360-SLR Document 401-10 Filed 05/13/2008 Page 20 of 90

systems used by others, in which staging is based primarily on urinary albumin excretion (158). Studies have found decreased GFR in the absence of increase urine albumin excretion in a substantial percentage of adults with diabetes (159,160). Thus, these studies demonstrate that significant decline in GFR may be noted in adults with type 1 and type 2 diabetes in the absence of increased urine albumin excretion. It is now clear that stage 3 or higher CKD (GFR <60 ml/min per 1.73 m^2) occurs in the absence of urine albumin excretion in a substantial proportion of adults with diabetes. Screening this population for increased urine albumin excretion alone, therefore, will miss a considerable number of CKD cases (158).

View this table: Table 9— Stages of CKD
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Serum creatinine should be measured at least annually for the estimation of GFR in all adults with diabetes regardless of the degree of urine albumin excretion. Serum creatinine alone should not be used as a measure of kidney function, but used to estimate GFR and stage the level of CKD. The GFR can be easily estimated using formulae like the Cockroft-Gault formula or a newer prediction formula developed by Levey et al. (161) using data collected from the MDRD (Modification of Diet and Renal Disease) study. Estimated GFR can easily be calculated by going to www.kidney.org/professionals/kdoqi/gfr_calculator.cfm.

The role of annual microalbumuria assessment is less clear after diagnosis of microalbuminuria and institution of ACE inhibitor or ARB therapy and blood pressure control. Most experts, however, recommend continued surveillance to assess both response to therapy and progression of disease. Some experts suggest that reducing urine microalbuminuria to the normal or near-normal range, if possible, may improve renal and cardiovascular prognosis. This approach has not been formally evaluated in prospective trials.

Consider referral to a physician experienced in the care of diabetic renal disease either when the GFR has fallen to <60 ml/min per 1.73 m^2 or if difficulties occur in the management of hypertension or hyperkalemia. It is suggested that consultation with a nephrologist be obtained when the GFR is <30 ml/min per 1.73 m^2. Early referral of such patients has been found to reduce cost and improve quality of care and keep people off dialysis longer (162,163).

C. Retinopathy screening and treatment

▲ TOP
▲ INTRODUCTION
▲ I. CLASSIFICATION AND DIAGNOSIS
▲ II. SCREENING FOR DIABETES
▲ III. DETECTION AND DIAGNOSIS...

Recommendations
General recommendations

- Optimal glycemic control can substantially

reduce the risk and progression of diabetic retinopathy. (A)
- Optimal blood pressure control can reduce the risk and progression of diabetic retinopathy. (A)
- Aspirin therapy does not prevent retinopathy or increase the risks of hemorrhage. (A)

Screening

- Adults and adolescents with type 1 diabetes should have an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist within 3–5 years after the onset of diabetes. (B)
- Patients with type 2 diabetes should have an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist shortly after the diagnosis of diabetes. (B)
- Subsequent examinations for type 1 and type 2 diabetic patients should be repeated annually by an ophthalmologist or optometrist. Less frequent exams (every 2–3 years) may be considered in the setting of a normal eye exam. Examinations will be required more frequently if retinopathy is progressing. (B)
- Women who are planning pregnancy or who have become pregnant should have a comprehensive eye examination and should be counseled on the risk of development and/or progression of diabetic retinopathy. Eye examination should occur in the first trimester with close follow-up throughout pregnancy and for 1 year postpartum. This guideline does not apply to women who develop GDM because such individuals are not at increased risk for diabetic retinopathy. (B)

Treatment

- Laser therapy can reduce the risk of vision loss in patients with high-risk characteristics (HRCs). (A)
- Promptly refer patients with any level of macular edema, severe NPDR, or any PDR to an ophthalmologist who is knowledgeable and experienced in the management and treatment of diabetic retinopathy. (A)

Diabetic retinopathy is a highly specific vascular complication of both type 1 and type 2 diabetes. The prevalence of retinopathy is strongly related to the duration of diabetes. Diabetic retinopathy is estimated to be the most frequent cause of new cases of blindness among adults aged 20–74 years. Glaucoma, cataracts, and other disorders of the eye may occur earlier in people with diabetes and should also be evaluated.

Intensive diabetes management with the goal of achieving near normoglycemia has been shown in large

prospective randomized studies to prevent and/or delay the onset of diabetic retinopathy (27,32,33). In addition to glycemic control, several other factors seem to increase the risk of retinopathy. The presence of nephropathy is associated with retinopathy. High blood pressure is an established risk factor for the development of macular edema and is associated with the presence of PDR. Lowering blood pressure, as demonstrated by the UKPDS, has been shown to decrease the progression of retinopathy. Several case series and a controlled prospective study suggest that pregnancy in type 1 diabetic patients may aggravate retinopathy (164). During pregnancy and 1 year postpartum, retinopathy may be transiently aggravated; laser photocoagulation surgery can minimize this risk (165).

Patients with type 1 diabetes should have an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist within 5 years after the onset of diabetes. Patients with type 2 diabetes should have an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist shortly after the diagnosis of diabetes. Subsequent examinations for type 1 and type 2 diabetic patients should be repeated annually by an ophthalmologist or optometrist who is knowledgeable and experienced in diagnosing the presence of diabetic retinopathy and is aware of its management. Less frequent exams (every 2–3 years) may be considered with the advice of an eye care professional in the setting of a normal eye exam (166–168). Examinations will be required more frequently if retinopathy is progressing.

Examinations can also be done by the taking of retinal photographs (with or without dilation of the pupil) and having these read by experienced experts in this field. In-person exams are still necessary when the photos are unacceptable and for follow-up of abnormalities detected. This technology has it greatest potential in areas where qualified eye care professionals are not available. Results of eye examinations should be documented and transmitted to the referring health care professional.

One of the main motivations for screening for diabetic retinopathy is the established efficacy of laser photocoagulation surgery in preventing visual loss. Two large National Institutes of Health–sponsored trials, the Diabetic Retinopathy Study (DRS) and the Early Treatment Diabetic Retinopathy Study (ETDRS), provide the strongest support for the therapeutic benefit of photocoagulation surgery.

The DRS tested whether scatter (panretinal) photocoagulation surgery could reduce the risk of vision loss from PDR. Severe visual loss (i.e., best acuity of 5/200 or worse) was seen in 15.9% of untreated vs. 6.4% of treated eyes. The benefit was greatest among patients whose baseline evaluation revealed HRCs (chiefly disc neovascularization or vitreous hemorrhage with any retinal neovascularization). Of control eyes with HRCs, 26% progressed to severe visual loss vs. 11% of treated eyes. Given the risk of a modest loss of visual acuity and of contraction of visual field from panretinal laser surgery, such therapy has been primarily recommended for eyes approaching or reaching HRCs.

The ETDRS established the benefit of focal laser photocoagulation surgery in eyes with macular edema, particularly those with clinically significant macular edema. In patients with clinically significant macular edema after 2 years, 20% of untreated eyes had a doubling of the visual angle (e.g., 20/50 to 20/100) compared with 8% of treated eyes. Other results from the ETDRS indicate that, provided careful follow-up can be maintained, scatter photocoagulation surgery is not recommended for eyes with

mild or moderate NPDR. When retinopathy is more severe, scatter photocoagulation surgery should be considered, and usually should not be delayed, if the eye has reached the high-risk proliferative stage. In older-onset patients with severe NPDR or less-than-high-risk PDR, the risk of severe visual loss and vitrectomy is reduced ~50% by laser photocoagulation surgery at these earlier stages.

Laser photocoagulation surgery in both the DRS and the ETDRS was beneficial in reducing the risk of further visual loss, but generally not beneficial in reversing already diminished acuity. This preventive effect and the fact that patients with PDR or macular edema may be asymptomatic provide strong support for a screening program to detect diabetic retinopathy.

For a detailed review of the evidence and further discussion, see the ADA's technical review and position statement on this subject (169,170).

D. Neuropathy screening and treatment (171,172)

Recommendations

- All patients should be screened for distal symmetric polyneuropathy (DPN) at diagnosis and at least annually thereafter, using simple clinical tests. (A)
- Electrophysiological testing is rarely ever needed, except in situations where the clinical features are atypical. (E)
- Once the diagnosis of DPN is established, special foot care is appropriate for insensate feet to decrease the risk of amputation. (B)
- Simple inspection of insensate feet should be performed at 3- to 6-month intervals. An abnormality should trigger referral for special footwear, preventive specialist, or podiatric care. (B)
- Screening for autonomic neuropathy should be instituted at diagnosis of type 2 diabetes and 5 years after the diagnosis of type 1 diabetes. Special electrophysiological testing for autonomic neuropathy is rarely needed and may not affect management and outcomes. (E)
- Education of patients about self-care of the feet and referral for special shoes/inserts are vital components of patient management. (B)
- A wide variety of medications is recommended for the relief of specific symptoms related to autonomic neuropathy and are recommended, as they improve the quality of life of the patient. (E)

Case 1:05-cv-00360-SLR Document 401-10 Filed 05/13/2008 Page 30 of 50

The diabetic neuropathies are heterogeneous with diverse clinical manifestations. They may be focal or diffuse. Most common among the neuropathies are chronic sensorimotor DPN and autonomic neuropathy. Although DPN is a diagnosis of exclusion, complex investigations to exclude other conditions are rarely needed.

The early recognition and appropriate management of neuropathy in the patient with diabetes is important for a number of reasons: *1*) nondiabetic neuropathies may be present in patients with diabetes and may be treatable; *2*) a number of treatment options exist for symptomatic diabetic neuropathy; *3*) up to 50% of DPN may be asymptomatic and patients are at risk of insensate injury to their feet; *4*) autonomic neuropathy may involve every system in the body; and *5*) cardiovascular autonomic neuropathy causes substantial morbidity and mortality. Specific treatment for the underlying nerve damage is currently not available, other than improved glycemic control, which may slow progression but rarely reverses neuronal loss. Effective symptomatic treatments are available for the manifestations of DPN and autonomic neuropathy.

Diagnosis of neuropathy

Patients with diabetes should be screened annually for DPN using tests such as pinprick sensation, temperature and vibration perception (using a 128-Hz tuning fork), and 10-g monofilament pressure sensation at the distal plantar aspect of both great toes and ankle reflexes. Combinations of more than one test have >87% sensitivity in detecting DPN. Loss of 10-g monofilament perception and reduced vibration perception predict foot ulcers. A minimum of one clinical test should be carried out annually, and the use of two tests will increase diagnostic ability.

Focal and multifocal neuropathy assessment requires clinical examination in the area related to the neurological symptoms.

Diabetic autonomic neuropathy (173)

The symptoms of autonomic dysfunction should be elicited carefully during the history and review of systems, particularly since many of these symptoms are potentially treatable. Major clinical manifestations of diabetic autonomic neuropathy include resting tachycardia, exercise intolerance, orthostatic hypotension, constipation, gastroparesis, erectile dysfunction, sudomotor dysfunction, impaired neurovascular function, "brittle diabetes," and hypoglycemic autonomic failure.

Cardiovascular autonomic neuropathy is the most studied and clinically important form of diabetic autonomic neuropathy. Cardiac autonomic neuropathy may be indicated by resting tachycardia (>100 bpm), orthostasis (a fall in systolic blood pressure >20 mmHg upon standing), or other disturbances in autonomic nervous system function involving the skin, pupils, or gastrointestinal and genitourinary systems.

Gastrointestinal disturbances (e.g., esophageal enteropathy, gastroparesis, constipation, diarrhea, fecal incontinence) are common, and any section of the gastrointestinal tract may be affected. Gastroparesis should be suspected in individuals with erratic glucose control. Upper-gastrointestinal symptoms should lead to consideration of all possible causes, including autonomic dysfunction. Evaluation of solid-phase

DJA-1428

Case 1:05-cv-00360-SLR Document 401-10 Filed 05/13/2008 Page 31 of 50

gastric emptying using double-isotope scintigraphy may be done if symptoms are suggestive, but test results often correlate poorly with symptoms. Barium studies or referral for endoscopy may be required to rule out structural abnormalities. Constipation is the most common lower-gastrointestinal symptom but can alternate with episodes of diarrhea. Endoscopy may be required to rule out other causes.

Diabetic autonomic neuropathy is also associated with genitourinary tract disturbances, including bladder and/or sexual dysfunction. Evaluation of bladder dysfunction should be performed for individuals with diabetes who have recurrent urinary tract infections, pyelonephritis, incontinence, or a palpable bladder. In men, diabetic autonomic neuropathy may cause loss of penile erection and/or retrograde ejaculation.

Symptomatic treatments
DPN
The first step in management of patients with DPN should be to aim for stable and optimal glycemic control. Although controlled trial evidence is lacking, several observational studies suggest that neuropathic symptoms improve not only with optimization of control, but also with the avoidance of extreme blood glucose fluctuations. Most patients will require pharmacological treatment for painful symptoms: many agents have efficacy confirmed in published randomized controlled trials, though none are specifically licensed for the management of painfulDPN. See Table 10 for examples of agents to treat DPN pain.

View this table: Table 10— Table of drugs to treat symptomatic DPN
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Treatment of autonomic neuropathy
A wide variety of agents are used to treat the symptoms of autonomic neuropathy, including metoclopramide for gastroparesis and several medications for bladder and erectile dysfunction. These treatments are frequently used to provide symptomatic relief to patients. Although they do not change the underlying pathology and natural history of the disease process, their use is recommended due to the impact they may have on the quality of life of the patient.

E. Foot care

Recommendations

- Perform a comprehensive foot examination and provide foot self-care education annually on patients with diabetes to identify risk factors predictive of ulcers and amputations. (B)
- The foot examination can be accomplished in a

primary care setting and should include the use of a monofilament, tuning fork, palpation, and a visual examination. (B)

- A multidisciplinary approach is recommended for individuals with foot ulcers and high-risk feet, especially those with a history of prior ulcer or amputation. (B)
- Refer patients who smoke or with prior lower-extremity complications to foot care specialists for ongoing preventive care and life-long surveillance. (C)
- Initial screening for peripheral arterial disease (PAD) should include a history for claudication and an assessment of the pedal pulses. Consider obtaining an ankle-brachial index (ABI), as many patients with PAD are asymptomatic. (C)
- Refer patients with significant claudication or a positive ABI for further vascular assessment and consider exercise, medications, and surgical options. (C)

Amputation and foot ulceration are the most common consequences of diabetic neuropathy and major causes of morbidity and disability in people with diabetes. Early recognition and management of independent risk factors can prevent or delay adverse outcomes.

The risk of ulcers or amputations is increased in people who have had diabetes >10 years, are male, have poor glucose control, or have cardiovascular, retinal, or renal complications. The following foot-related risk conditions are associated with an increased risk of amputation:

- Peripheral neuropathy with loss of protective sensation
- Altered biomechanics (in the presence of neuropathy)
- Evidence of increased pressure (erythema, hemorrhage under a callus)
- Bony deformity
- Peripheral vascular disease (decreased or absent pedal pulses)
- A history of ulcers or amputation
- Severe nail pathology

All individuals with diabetes should receive an annual foot examination to identify high-risk foot conditions. This examination should include assessment of protective sensation, foot structure and biomechanics, vascular status, and skin integrity. People with one or more high-risk foot condition should be evaluated more frequently for the development of additional risk factors. People with neuropathy should have a visual inspection of their feet at every visit with a health care professional. Evaluation of neurological status in the low-risk foot should include a quantitative somatosensory threshold test, using the Semmes-Weinstein 5.07 (10-g) monofilament. The skin should be assessed for integrity, especially between the toes and under the metatarsal heads. The presence of erythema,

warmth, or callus formation may indicate areas of tissue damage with impending breakdown. Bony deformities, limitation in joint mobility, and problems with gait and balance should be assessed.

People with neuropathy or evidence of increased plantar pressure may be adequately managed with well-fitted walking shoes or athletic shoes. Patients should be educated on the implications of sensory loss and the ways to substitute other sensory modalities (hand palpation, visual inspection) for surveillance of early problems. People with evidence of increased plantar pressure (e.g., erythema, warmth, callus, or measured pressure) should use footwear that cushions and redistributes the pressure. Callus can be debrided with a scalpel by a foot care specialist or other health professional with experience and training in foot care. People with bony deformities (e.g., hammertoes, prominent metatarsal heads, bunions) may need extra-wide shoes or depth shoes. People with extreme bony deformities (e.g., Charcot foot) who cannot be accommodated with commercial therapeutic footwear may need custom-molded shoes.

Initial screening for PAD should include a history for claudication and an assessment of the pedal pulses. Consider obtaining an ABI, as many patients with PAD are asymptomatic. Refer patients with significant or a positive ABI for further vascular assessment and consider exercise, medications, and surgical options (174).

Patients with diabetes and high-risk foot conditions should be educated regarding their risk factors and appropriate management. Patients at risk should understand the implications of the loss of protective sensation, the importance of foot monitoring on a daily basis, the proper care of the foot, including nail and skin care, and the selection of appropriate footwear. The patient's understanding of these issues and their physical ability to conduct proper foot surveillance and care should be assessed. Patients with visual difficulties, physical constraints preventing movement, or cognitive problems that impair their ability to assess the condition of the foot and to institute appropriate responses will need other people, such as family members, to assist in their care. Patients at low risk may benefit from education on foot care and footwear.

For a detailed review of the evidence and further discussion, see the ADA's technical review and position statement on this subject (175,176).

Problems involving the feet, especially ulcers and wound care, may require care by a podiatrist, orthopedic surgeon, or rehabilitation specialist experienced in the management of individuals with diabetes. For a complete discussion on wound care, see the ADA's consensus statement on diabetic foot wound care (177).

VII. DIABETES CARE IN SPECIFIC POPULATIONS

▲ TOP
▲ INTRODUCTION
▲ I. CLASSIFICATION AND DIAGNOSIS
▲ II. SCREENING FOR DIABETES

A. Children and adolescents

1. Type 1 diabetes

Although approximately three-quarters of all cases of type 1 diabetes are diagnosed in individuals <18 years of age, historically ADA recommendations for management of type 1 diabetes have pertained most directly to adults with type 1 diabetes. Because children are not simply "small adults," it is appropriate to consider the unique aspects of care and management of children and adolescents with type 1 diabetes. Children with diabetes differ from adults in many respects, including insulin sensitivity related to sexual maturity, physical growth, ability to provide self-care, and unique neurologic vulnerability to hypoglycemia. Attention to such issues as family dynamics, developmental stages, and physiologic differences related to sexual maturity all are essential in developing and implementing an optimal diabetes regimen. Although current recommendations for children and adolescents are less likely to be based on evidence derived from rigorous research because of current and historical restraints placed on conducting research in children, expert opinion and a review of available and relevant experimental data are summarized in a recent ADA statement (178). The following represents a summary of recommendations and guidelines pertaining specifically to the care and management of children and adolescents that are included in that document.

Ideally, the care of a child or adolescent with type 1 diabetes should be provided by a multidisciplinary team of specialists trained in the care of children with pediatric diabetes, although this may not always be possible. At the very least, education of the child and family should be provided by health care providers trained and experienced in childhood diabetes and sensitive to the challenges posed by diabetes in this age-group. At the time of initial diagnosis, it is essential that diabetes education be provided in a timely fashion, with the expectation that the balance between adult supervision and self-care should be defined by, and will evolve according to, physical, psychological, and emotional maturity. MNT should be provided at diagnosis, and at least annually thereafter, by an individual experienced with the nutritional needs of the growing child and the behavioral issues that have an impact on adolescent diets.

a. Glycemic control.

While current standards for diabetes management reflect the need to maintain glucose control as near to normal as safely possible, special consideration must be given to the unique risks of hypoglycemia in young children. Glycemic goals need to be modified to take into account the fact that most children <6 or 7 years of age have a form of "hypoglycemic unawareness," in that counterregulatory mechanisms are immature, and young children lack the cognitive capacity to recognize and respond to hypoglycemic symptoms, placing them at greater risk for hypoglycemia and its sequelae. In addition, extensive evidence indicates that near normalization of blood glucose levels is seldom attainable in children and

adolescents after the honeymoon (remission) period. The A1C level achieved in the "intensive" adolescent cohort of the DCCT group was >1% higher than that achieved for older patients and current ADA recommendations for patients in general (179). However, the increased frequency of use of basal bolus regimens (including insulin pumps) in youth from infancy through adolescence has been associated with more children reaching ADA blood glucose targets (180,181).

In selecting glycemic goals, the benefits of achieving a lower A1C must be weighed against the unique risks of hypoglycemia and the disadvantages of targeting a higher, though more achievable, goal that may not promote optimal long-term health outcomes. Age-specific glycemic and A1C goals are presented in Table 11.

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Table 11— Plasma blood glucose and A1C goals for type 1 diabetes by age-group

b. Screening and management of chronic complications in children and adolescents with type 1 diabetes.

i. *Nephropathy*

Recommendations

- Annual screening for microalbuminuria should be initiated once the child is 10 years of age and has had diabetes for 5 years. Screening may be done with a random spot urine sample analyzed for microalbumin-to-creatinine ratio. (E)
- Confirmed, persistently elevated microalbumin levels should be treated with an ACE inhibitor, titrated to normalization of microalbumin excretion (if possible). (E)

ii. *Hypertension*

Recommendations

- Treatment of high-normal blood pressure (systolic or diastolic blood pressure consistently above the 90th percentile for age, sex, and height) should include dietary intervention and exercise, aimed at weight control and increased physical activity, if appropriate. If target blood pressure is not reached within 3–6 months of lifestyle intervention, pharmacologic treatment should be initiated. (E)
- Pharmacologic treatment of hypertension (systolic or diastolic blood pressure consistently above the 95th percentile for age, sex, and height or consistently greater than 130/80 mmHg, if 95% exceeds that value) should be initiated as soon as the diagnosis is confirmed. (E)
- ACE inhibitors should be considered for the initial treatment of hypertension. (E)

Hypertension in childhood is defined as an average systolic or diastolic blood pressure ≥95th percentile for age, sex, and height percentile measured on at least three separate days. "High-normal" blood

pressure is defined as an average systolic or diastolic blood pressure ≥90th but <95th percentile for age, sex, and height percentile measured on at least 3 separate days. Normal blood pressure levels for age, sex, and height and appropriate methods for determinations are available online at www.nhlbi.nih.gov/health/prof/heart/hbp/hbp_ped.pdf.

iii. *Dyslipidemia*

Recommendations

Screening

- Prepubertal children: a fasting lipid profile should be performed on all children >2 years of age at the time of diagnosis (after glucose control has been established) if there is a family history of hypercholesterolemia (total cholesterol >240 mg/dl), if there is a history of a cardiovascular event before age 55 years, or if family history is unknown. If family history is not of concern, then the first lipid screening should be performed at puberty (>12 years). If values are within the accepted risk levels (LDL <100 mg/dl [2.6 mmol/l]), a lipid profile should be repeated every 5 years. (E)
- Pubertal children (>12 years of age): a fasting lipid profile should be performed at the time of diagnosis (after glucose control has been established). If values fall within the accepted risk levels (LDL <100 mg/dl [2.6 mmol/l]), the measurement should be repeated every 5 years. (E)
- If lipids are abnormal, annual monitoring is recommended in both age-groups. (E)

Treatment

- Treatment should be based on fasting lipid levels (mainly LDL) obtained after glucose control is established. (E)
- Initial therapy should consist of optimization of glucose control and MNT aimed at a decrease in the amount of saturated fat in the diet. (E)
- The addition of a pharmacologic lipid-lowering agents is recommended for LDL >160 mg/dl (4.1 mmol/l), and is also recommended in patients who have LDL cholesterol values of 130–159 mg/dl (3.4–4.1 mmol/l) based on the patient's CVD risk profile, after failure of MNT and lifestyle changes. (E)
- The goal of therapy is an LDL value <100 mg/dl (2.6 mmol/l). (E)

iv. *Retinopathy*

Recommendations

- The first ophthalmologic examination should be obtained once the child is ≥10 years of age and has had diabetes for 3–5 years. (E)
- After the initial examination, annual routine follow-up is generally recommended. Less frequent examinations may be acceptable on the advice of an eye care professional. (E)

Although retinopathy most commonly occurs after the onset of puberty and after 5–10 years of diabetes duration, it has been reported in prepubertal children and with diabetes duration of only 1–2 years.

Referrals should be made to eye care professionals with expertise in diabetic retinopathy, an understanding of the risk for retinopathy in the pediatric population, and experience in counseling the pediatric patient and family on the importance of early prevention/intervention.

v. *Celiac disease*

Recommendations

- Children with positive antibodies should be referred to a gastroenterologist for evaluation. (E)
- Children with confirmed celiac disease should have consultation with a dietitian and placed on a gluten-free diet. (E)
- Patients with type 1 diabetes who are or who become symptomatic for celiac disease should be screened, using tTG antibodies, or anti-EMA, with documentation of normal serum IgA levels. (E)

Celiac disease is an immune-mediated disorder that occurs with increased frequency in patients with type 1 diabetes (1–16% of individuals compared with 0.3–1% in the general population) (182,183). Symptoms of celiac disease include diarrhea, weight loss or poor weight gain, growth failure, abdominal pain, chronic fatigue, malnutrition due to malabsorption, and other gastrointestinal problems.

c. Other issues.

A major issue deserving emphasis in this age-group is that of "adherence." No matter how sound the medical regimen, it can only be as good as the ability of the family and/or individual to implement it. Family involvement in diabetes remains an important component of optimal diabetes management throughout childhood and into adolescence. Health care providers who care for children and adolescents, therefore, must be capable of evaluating the behavioral, emotional, and psychosocial factors that interfere with implementation and then must work with the individual and family to resolve problems that occur and/or to modify goals as appropriate.

Since a sizable portion of a child's day is spent in school, close communication with school or day care personnel is essential for optimal diabetes management. Information should be supplied to school personnel, so that they may be made aware of the diagnosis of diabetes in the student and of the signs, symptoms, and treatment of hypoglycemia. In most cases it is imperative that blood glucose testing be performed at the school or day care setting before lunch and when signs or symptoms of abnormal blood glucose levels are present. Many children may require support for insulin administration by either injection or continuous subcutaneous insulin infusion (CSII) before lunch (and often also before breakfast) at school or in day care. For further discussion, see the ADA position statement (184) and the report from the NDEP (185).

2. Type 2 diabetes

Finally, the incidence of type 2 diabetes in adolescents has been shown to be increasing, especially in ethnic minority populations (186,187). Distinction between type 1 and type 2 diabetes in children can be difficult, since autoantigens and ketosis may be present in a substantial number of patients with otherwise straightforward type 2 diabetes (including obesity and acanthosis nigricans). Such a distinction at the time of diagnosis is critical since treatment regimens, educational approaches, and

Case 1:05-cv-00360-SLR Document 401-10 Filed 05/13/2008 Page 38 of 50

dietary counsel will differ markedly between the two diagnoses. It is recommended that screening for the comorbidities and complications of diabetes, including fasting lipid profile, and urine for microalbumin, be obtained at the time of diagnosis of type 2 diabetes. An ophthalmologic examination should be considered. The ADA consensus statement (11) provides guidance on the prevention, screening, and treatment of type 2 diabetes, as well as its comorbidities, in young people.

B. Preconception care

Recommendations

- A1C levels should be normal or as close to normal as possible (<1% above the upper limits of normal) in an individual patient before conception is attempted. (B)
- All women with diabetes and child-bearing potential should be educated about the need for good glucose control before pregnancy. They should participate in family planning. (E)
- Women with diabetes who are contemplating pregnancy should be evaluated and, if indicated, treated for diabetic retinopathy, nephropathy, neuropathy, and CVD. (E)
- Among the drugs commonly used in the treatment of patients with diabetes, statins are pregnancy category X and should be discontinued before conception if possible. Based on recent research, ACE inhibitors also should be discontinued before conception (187a). ARBs are category C in the first trimester (maternal benefit may outweigh fetal risk in certain situations), but category D in later pregnancy, and should generally be discontinued before pregnancy. Among the oral antidiabetic agents, metformin and acarbose are classified as category B and all others as category C; potential risks and benefits of oral antidiabetic agents in the preconception period must be carefully weighed, recognizing that sufficient data are not available to establish the safety of these agents in pregnancy. They should generally be discontinued in pregnancy. (E)

Major congenital malformations remain the leading cause of mortality and serious morbidity in infants of mothers with type 1 and type 2 diabetes. Observational studies indicate that the risk of malformations increases continuously with increasing maternal glycemia during the first 6–8 weeks of gestation, as defined by first-trimester A1C concentrations. There is no threshold for A1C values above which the risk begins or below which it disappears. However, malformation rates above the 1–2% background rate seen in nondiabetic pregnancies appear to be limited to pregnancies in which first-trimester A1C

DJA-1436

concentrations are >1% above the normal range for a nondiabetic pregnant woman.

Preconception care of diabetes appears to reduce the risk of congenital malformations. Five nonrandomized studies have compared rates of major malformations in infants between women who participated in preconception diabetes care programs and women who initiated intensive diabetes management after they were already pregnant. The preconception care programs were multidisciplinary and designed to train patients in diabetes self-management with diet, intensified insulin therapy, and SMBG. Goals were set to achieve normal blood glucose concentrations, and >80% of subjects achieved normal A1C concentrations before they became pregnant (188–192). In all five studies, the incidence of major congenital malformations in women who participated in preconception care (range 1.0–1.7% of infants) was much lower than the incidence in women who did not participate (range 1.4–10.9% of infants). One limitation of these studies is that participation in preconception care was self-selected by patients rather than randomized. Thus, it is impossible to be certain that the lower malformation rates resulted fully from improved diabetes care. Nonetheless, the overwhelming evidence supports the concept that malformations can be reduced or prevented by careful management of diabetes before pregnancy.

Planned pregnancies greatly facilitate preconception diabetes care. Unfortunately, nearly two-thirds of pregnancies in women with diabetes are unplanned, leading to a persistent excess of malformations in infants of diabetic mothers. To minimize the occurrence of these devastating malformations, standard care for all women with diabetes who have child-bearing potential should include *1*) education about the risk of malformations associated with unplanned pregnancies and poor metabolic control and *2*) use of effective contraception at all times, unless the patient is in good metabolic control and actively trying to conceive.

Women contemplating pregnancy need to be seen frequently by a multidisciplinary team experienced in the management of diabetes before and during pregnancy. Teams may vary but should include a diabetologist, an internist or a family physician, an obstetrician, a diabetes educator, a dietitian, a social worker, and other specialists as necessary. The goals of preconception care are to *1*) integrate the patient into the management of her diabetes, *2*) achieve the lowest A1C test results possible without excessive hypoglycemia, *3*) assure effective contraception until stable and acceptable glycemia is achieved, and *4*) identify, evaluate, and treat long-term diabetic complications such as retinopathy, nephropathy, neuropathy, hypertension, and CAD.

For further discussion, see the ADA's technical review (193) and position statement (194) on this subject.

C. Older individuals

▲ TOP
▲ INTRODUCTION
▲ I. CLASSIFICATION AND DIAGNOSIS
▲ II. SCREENING FOR DIABETES

Diabetes is an important health condition for the aging population; at least 20% of patients over the age of 65 years have diabetes. The number of older individuals

with diabetes can be expected to grow rapidly in the coming decades. A recent publication (195) contains evidence-based guidelines produced in conjunction with the American Geriatric Society. This document contains an excellent discussion of this area, and specific guidelines and language from it have been incorporated below. Unfortunately, there are no long-term studies in individuals >65 years of age demonstrating the benefits of tight glycemic control, blood pressure, and lipid control. Older individuals with diabetes have higher rates of premature death, functional disability, and coexisting illnesses such as hypertension, CHD, and stroke than those without diabetes. Older adults with diabetes are also at greater risk than other older adults for several common geriatric syndromes, such as polypharmacy, depression, cognitive impairment, urinary incontinence, injurious falls, and persistent pain.

The care of older adults with diabetes is complicated by their clinical and functional heterogeneity. Some older individuals developed diabetes in middle age and face years of comorbidity; others who are newly diagnosed may have had years of undiagnosed comorbidity or few complications from the disease. Some older adults with diabetes are frail and have other underlying chronic conditions, substantial diabetes-related comorbidity, or limited physical or cognitive functioning, but other older individuals with diabetes have little comorbidity and are active. Life expectancies are also highly variable for this population. Clinicians caring for older adults with diabetes must take this heterogeneity into consideration when setting and prioritizing treatment goals.

All this having been said, patients who can be expected to live long enough to reap the benefits of long-term intensive diabetes management (~10 years) and who are active, cognitively intact, and willing to undertake the responsibility of self-management should be encouraged to do so and be treated using the stated goals for younger adults with diabetes.

There is good evidence from middle-aged and older adults suggesting that multidisciplinary interventions that provide education on medication use, monitoring, and recognizing hypo- and hyperglycemia can significantly improve glycemic control. Although control of hyperglycemia is important, in older individuals with diabetes, greater reductions in morbidity and mortality may result from control of all cardiovascular risk factors rather than from tight glycemic control alone. There is strong evidence from clinical trials of the value of treating hypertension in the elderly. There is less evidence for lipid-lowering and aspirin therapy, although as diabetic patients have such an elevated risk for CVD, aggressive management of lipids and aspirin use when not contraindicated are reasonable interventions.

As noted above, for patients with advanced diabetes complications, life-limiting comorbid illness, or cognitive or functional impairment, it is reasonable to set less intensive glycemic target goals. These patients are less likely to benefit from reducing the risk of microvascular complications and more likely to suffer serious adverse effects from hypoglycemia. Patients with poorly controlled diabetes may be subject to acute complications of diabetes, including hyperglycemic hyperosmolar coma. Older patients can be treated with the same drug regimens as younger patients, but special care is required in prescribing and monitoring drug therapy. Metformin is often contraindicated because of renal insufficiency or heart failure. Sulfonylureas and other insulin secretagogues can cause hypoglycemia. Insulin can also cause hypoglycemia as well as require good visual and motor skills and cognitive ability of the patient or a caregiver. TZDs should not be used in patients with CHF (New York Heart Association class III and IV). Drugs should be started at the lowest dose and titrated up gradually until targets are reached or side effects develop. As with blood pressure and lipid management, the potential benefits must always be weighed against potential risks.

VIII. DIABETES CARE IN SPECIFIC SETTINGS

A. Diabetes care in the hospital

Recommendations

- All patients with diabetes admitted to the hospital should be identified in the medical record as having diabetes. (E)
- All patients with diabetes should have an order for blood glucose monitoring, with results available to all members of the health care team. (E)
- Goals for blood glucose levels:
  - Critically ill patients: blood glucose levels should be kept as close to 110 mg/dl (6.1 mmol/l) as possible and generally <180 mg/dl (10 mmol/l). These patients will usually require intravenous insulin. (B)
  - Non–critically ill patients: premeal blood glucose levels should be kept as close to 90–130 mg/dl (5.0–7.2 mmol/l; midpoint of range 110 mg/dl) as possible given the clinical situation and postprandial blood glucose levels <180 mg/dl. Insulin should be used as necessary. (E)
  - Due to concerns regarding the risk of hypoglycemia, some institutions may consider these blood glucose levels to be overly aggressive for initial targets. Through quality improvement, glycemic goals should systematically be reduced to the recommended levels. (E)

- Scheduled prandial insulin doses should be given in relation to meals and should be adjusted according to point-of-care glucose levels. The traditional sliding-scale insulin regimens are ineffective as monotherapy and are not recommended. (C)
- Using correction dose or "supplemental" insulin to correct premeal hyperglycemia in addition to scheduled prandial and basal insulin is recommended. (C)
- A plan for treating hypoglycemia should be established for each patient. Episodes of hypoglycemia in the hospital should be tracked. (E)
- All patients with diabetes admitted to the hospital should have an A1C obtained for discharge planning if the result of testing in the previous 2–3 months is not available. (E)
- A diabetes education plan including "survival skills education" and follow-up should be developed for each patient. (E)
- Patients with hyperglycemia in the hospital who do not have a diagnosis of diabetes should have appropriate plans for follow-up testing and care documented at discharge. (E)

The management of diabetes in the hospital is extensively reviewed in an ADA technical review by Clement et al. (196). This review forms the basis for these guidelines. In addition, the American Association of Clinical Endocrinologists held a conference on this topic (197), and the recommendations from this meeting (198) were also carefully reviewed and discussed in the formulation of the guidelines that follow. The management of diabetes in the hospital is generally considered secondary in importance compared with the condition that prompted admission (199).

Patients with hyperglycemia fall into three categories:

- Medical history of diabetes: diabetes has been previously diagnosed and acknowledged by the patient's treating physician.
- Unrecognized diabetes: hyperglycemia (fasting blood glucose 126 mg/dl or random blood glucose 200 mg/dl) occurring during hospitalization and confirmed as diabetes after hospitalization by standard diagnostic criteria but unrecognized as diabetes by the treating physician during hospitalization.
- Hospital-related hyperglycemia: hyperglycemia (fasting blood glucose 126 mg/dl or random blood glucose ≥200 mg/dl) occurring during the hospitalization that reverts to normal after hospital discharge.

The prevalence of diabetes in hospitalized adult patients is not precisely known. In the year 2000, 12.4% of hospital discharges in the U.S. listed diabetes as a diagnosis. The prevalence of diabetes in hospitalized adults is conservatively estimated at 12–25%, depending on the thoroughness used in identifying patients. Patients presenting to hospitals may have diabetes, unrecognized diabetes, or hospital-related hyperglycemia. Using the A1C test may be a valuable case-finding tool for identifying diabetes in hospitalized patients. In the year 2003, there were 5.1 million hospitalizations for diabetes as any-listed diagnosis. By way of comparison, in 1980 there were 2.2 million hospitalizations for those having diabetes (200).

Case 1:05-cv-00360-SLR Document 401-10 Filed 05/13/2008 Page 43 of 90

A rapidly growing body of literature supports targeted glucose control in the hospital setting with potential for improved mortality, morbidity, and health care economic outcomes. Hyperglycemia in the hospital may result from stress, decompensation of type 1 diabetes, type 2 diabetes, or other forms of diabetes and/or may be iatrogenic due to administration or withholding of pharmacologic agents, including glucocorticoids, vasopressors, etc. Distinction between decompensated diabetes and stress hyperglycemia is often not made.

1. Blood glucose targets

a. General medicine and surgery.

Observational studies suggest an association between hyperglycemia and increased mortality. General medical and surgical patients with a blood glucose value(s) >220 mg/dl (12.2 mmol/l) have higher infection rates (201).

When admissions on general medicine and surgery units were studied, patients with new hyperglycemia had significantly increased inhospital mortality, as did patients with known diabetes. In addition, length of stay was higher for the new hyperglycemic group, and both the patients with new hyperglycemia and those with known diabetes were more likely to require intensive care unit (ICU) care and transitional or nursing home care. Better outcomes were demonstrated in patients with fasting and admission blood glucose <126 mg/dl (7 mmol/l) and all random blood glucose levels <200 mg/dl (11.1 mmol/l) (202).

b. CVD and critical care.

The relationship of blood glucose levels and mortality in the setting of acute myocardial infarction (AMI) has been reported. A meta-analysis of 15 previously published studies compared in-hospital mortality and CHF in both hyper- and normoglycemic patients with and without diabetes. In subjects without known diabetes whose admission blood glucose was 109.8 mg/dl (6.1 mmol/l), the relative risk for in-hospital mortality was increased significantly. When diabetes was present and admission glucose 180 mg/dl (10 mmol/l), risk of death was moderately increased compared with patients who had diabetes but no hyperglycemia on admission (203). In another study (204), admission blood glucose values were analyzed in consecutive patients with AMI. Analysis revealed an independent association of admission blood glucose and mortality. The 1-year mortality rate was significantly lower in subjects with admission plasma glucose <100.8 mg/dl (5.6 mmol/l) than in those with plasma glucose 199.8 mg/dl (11 mmol/l).

It is important to note that these studies focused more on admission blood glucose as a predictor of outcomes rather than inpatient diabetes or glycemic management per se. Higher admission plasma glucose levels in patients with a prior history of diabetes could reflect the degree of glycemic control experienced in the outpatient setting, thus linking attention to outpatient glycemic control to outcomes in the inpatient population. In patients without a prior history of diabetes, this could represent case finding of patients previously undiagnosed with diabetes who have the disease, an unmasking of risk in a population at high risk for diabetes, or possibly more severe illness at admission.

In the first DIGAMI (Diabetes and Insulin-Glucose Infusion in Acute Myocardial Infarction) study (84,205), insulin-glucose infusion followed by subcutaneous insulin treatment in diabetic patients with

DJA-1441

AMI was examined. Intensive subcutaneous insulin therapy for ≥3 months improved long-term survival (84). Mean blood glucose in the intensive insulin intervention arm was 172.8 mg/dl (9.6 mmol/l) (compared with 210.6 mg/dl [11.7 mmol/l] in the "conventional" group). The broad range of blood glucose levels within each arm limits the ability to define specific blood glucose target thresholds.

Finally, two more recent studies (206,207) using an insulin-glucose infusion did not show a reduction in mortality in the intervention groups. However, in both of these studies, blood glucose levels were positively correlated with mortality.

c. Cardiac surgery.

Attainment of targeted glucose control in the setting of cardiac surgery is associated with reduced mortality and risk of deep sternal wound infections in cardiac surgery patients with diabetes (208,209) and supports the concept that perioperative hyperglycemia is an independent predictor of infection in patients with diabetes (210), with the lowest mortality in patients with blood glucose <150 mg/dl (8.3 mmol/l) (211).

d. Critical care.

A mixed group of patients with and without diabetes admitted to a surgical ICU were randomized to receive intensive insulin therapy (target blood glucose 80–110 mg/dl [4.4–6.1 mmol/l]). The mean blood glucose of 103 mg/dl (5.7 mmol/l) had reduced mortality during the ICU stay and decreased overall in-hospital mortality (85). Hospital and ICU survival were linearly associated with ICU glucose levels, with the highest survival rates occurring in patients achieving an average blood glucose <110 mg/dl (6.1 mmol/l) (212).

The same group subsequently studied a similar population of patients in a medical ICU (213). As in the SICU (Surgical Intensive Care Unit) study, one group received intensive insulin therapy [mean blood glucose 110 mg/dl (6.1 mmol/l)] while the other received conventional therapy [mean blood glucose 161 mg/dl (8.9 mmol/l). The group receiving the intensive therapy had reduced morbidity but not mortality among all patients in the MICU. However, death was reduced for those patients who were treated for longer than 3 days. These patients could not be identified before therapy.

2. Treatment options

a. Noninsulin glucose-lowering agents.

No large studies have investigated the potential roles of various oral agents on outcomes in hospitalized patients with diabetes. While the various classes of oral agents are commonly used in the outpatient setting with good response, their use in the inpatient setting presents some specific issues.

i. *Sulfonylureas and meglitinides*. The long action and predisposition to hypoglycemia in patients not consuming their normal nutrition serve as relative contraindications to routine use of sulfonylureas in the hospital for many patients (214). Sulfonylureas do not generally allow rapid dose adjustment to meet the changing inpatient needs. Sulfonylureas also vary in duration of action between individuals and likely vary in the frequency with which they induce hypoglycemia. While the two available meglitinides, repaglinide and neteglinide, theoretically would produce less hypoglycemia than sulfonylureas, lack of clinical trial data for these agents would preclude their use.

ii. *Metformin*. The major limitation to metformin use in the hospital is a number of specific contraindications to its use, many of which occur in the hospital. All of these contraindications relate to lactic acidosis, a potentially fatal complication of metformin therapy. The most common risk factors for lactic acidosis in metformin-treated patients are cardiac disease, including CHF, hypoperfusion, renal insufficiency, old age, and chronic pulmonary disease (215). Recent evidence continues to indicate lactic acidosis is a rare complication (216), despite the relative frequency of risk factors (217). However, in the hospital, where the risk for hypoxia, hypoperfusion, and renal insufficiency is much higher, it still seems prudent to avoid the use of metformin in most patients.

iii. *TZDs*. TZDs are not suitable for initiation in the hospital because of their delayed onset of effect. In addition, they do increase intravascular volume, a particular problem in those predisposed to CHF and potentially a problem for patients with hemodynamic changes related to admission diagnoses (e.g., acute coronary ischemia) or interventions common in hospitalized patients.

iv. *Pramlintide and exenatide*. These drugs work mainly by reducing postprandial hyperglycemia. Therefore, they would not be appropriate for patients not eating (NPO) or with reduced caloric consumption. Furthermore, it would generally be inappropriate to initiate these drugs in the inpatient setting due to all of the differences in normal food intake, in addition to the fact that both of these agents result in nausea as the most common side effect. In general, these agents should be initiated when the patient is not ill in the outpatient setting.

In summary, each of the major classes of oral agents has significant limitations for inpatient use. Additionally, they provide little flexibility or opportunity for titration in a setting where acute changes demand these characteristics. Therefore, insulin, when used properly, may have many advantages in the hospital setting.

b. Insulin.

The inpatient insulin regimen must be matched or tailored to the specific clinical circumstance of the individual patient. A recent meta-analysis concluded that insulin therapy in critically ill patients had a beneficial effect on short-term mortality in different clinical settings (218).

i. *Subcutaneous insulin therapy*. Subcutaneous insulin therapy may be used to attain glucose control in most hospitalized patients with diabetes. The components of the daily insulin dose requirement can be met by a variety of insulins, depending on the particular hospital situation. Subcutaneous insulin therapy is subdivided into programmed or scheduled insulin and supplemental or correction-dose insulin. Correction-dose insulin therapy is an important adjunct to scheduled insulin, both as a dose-finding strategy and as a supplement when rapid changes in insulin requirements lead to hyperglycemia. If correction doses are frequently required, it is recommended that the appropriate scheduled insulin doses be increased the following day to accommodate the increased insulin needs (219). There are no studies comparing human regular insulin with rapid-acting analogs for use as correction-dose insulin. However, due to the longer duration with human regular insulin, there is a greater risk of "insulin stacking" when the usual next blood glucose measurement is performed 4–6 h later.

Case 1:05-cv-00360-SLR Document 401-10 Filed 05/13/2008 Page 46 of 50

The traditional sliding-scale insulin regimens, usually consisting of regular insulin without any intermediate or long-acting insulins, have been shown to be ineffective when used as monotherapy in patients with an established insulin requirement (219–221). Problems cited with sliding-scale insulin regimens are that the sliding-scale regimen prescribed on admission is likely to be used throughout the hospital stay without modification (219). Second, sliding-scale insulin therapy treats hyperglycemia after it has already occurred, instead of preventing the occurrence of hyperglycemia. This "reactive" approach can lead to rapid changes in blood glucose levels, exacerbating both hyper- and hypoglycemia.

ii. *Intravenous insulin infusion.* The only method of insulin delivery specifically developed for use in the hospital is continuous intravenous infusion, using regular crystalline insulin. There is no advantage to using insulin lispro or aspart in an intravenous insulin infusion. The medical literature supports the use of intravenous insulin infusion in preference to the subcutaneous route of insulin administration for several clinical indications among nonpregnant adults. These include DKA and nonketotic hyperosmolar state; general preoperative, intraoperative, and postoperative care; the postoperative period following heart surgery; following organ transplantation; with cardiogenic shock; exacerbated hyperglycemia during high-dose glucocorticoid therapy; patients who are NPO or in critical care illness in general; and as a dose-finding strategy in anticipation of initiation or reinitiation of subcutaneous insulin therapy in type 1 or type 2 diabetes.

Many institutions use insulin infusion algorithms that can be implemented by nursing staff. Algorithms should incorporate the concept that maintenance requirements differ between patients and change over the course of treatment. Although numerous algorithms have been published, there have been no head-to-head comparisons, and thus no single algorithm can be recommended for an individual hospital. Ideally, intravenous insulin algorithms should consider both the current and previous glucose level, the rate of change of plasma glucose, and the current IV insulin infusion rate. For all algorithms, frequent bedside glucose testing is required but the ideal frequency is not known.

iii. *Transition from intravenous to subcutaneous insulin therapy*. There are no specific clinical trials examining how to best transition from intravenous to subcutaneous insulin or which patients with type 2 diabetes may be transitioned to oral agents. For those who will require subcutaneous insulin, it is necessary to administer short- or rapid-acting insulin subcutaneously 1–2 h before discontinuation of the intravenous insulin infusion. An intermediate- or long-acting insulin must be injected 2–3 h before discontinuing the insulin infusion. In transitioning from intravenous insulin infusion to subcutaneous therapy, the caregiver may order subcutaneous insulin with appropriate duration of action to be administered as a single dose or repeatedly to maintain basal effect until the time of day when the choice of insulin or analog preferred for basal effect normally would be provided.

3. Self-management in the hospital

Self-management in the hospital may be appropriate for competent adult patients who have a stable level of consciousness and reasonably stable known daily insulin requirements and successfully conduct self-management of diabetes at home, have physical skills appropriate to successfully self-administer insulin, perform SMBG, and have adequate oral intake. Appropriate patients are those already proficient in carbohydrate counting, use of multiple daily injections of insulin or insulin pump therapy, and sick-

DJA-1444

Case 1:05-cv-00360-SLR Document 401-10 Filed 05/13/2008 Page 47 of 50

day management. The patient and physician in consultation with nursing staff must agree that patient self-management is appropriate under the conditions of hospitalization. For patients who are selected for self-management in the hospital, it is important that basal and bolus doses of insulin with results of bedside glucose monitoring be recorded as part of the patient's hospital medical record.

While many institutions allow patients on an insulin pump to continue these devices in the hospital, others express concern regarding use of a device that nurses are unfamiliar with, particularly in patients who are not able to manage their own pump therapy. If a patient is too ill to self-manage either multiple daily injections or CSII, then appropriate subcutaneous doses can be calculated on the basis of their basal and bolus insulin doses during hospitalization with adjustments for changes in nutritional or metabolic status.

4. Preventing hypoglycemia

Hypoglycemia, especially in insulin-treated patients, is the leading limiting factor in the glycemic management of type 1 and type 2 diabetes (86). In the hospital, multiple additional risk factors for hypoglycemia are present, even among patients who are neither "brittle" nor tightly controlled. Patients who do not have diabetes may experience hypoglycemia in the hospital, in association with factors such as altered nutritional state, heart failure, renal or liver disease, malignancy, infection, or sepsis (222). Patients having diabetes may develop hypoglycemia in association with the same conditions (223). Additional triggering events leading to iatrogenic hypoglycemia include sudden reduction of corticosteroid dose, altered ability of the patient to self-report symptoms, reduction of oral intake, emesis, new NPO status, reduction of rate of administration of intravenous dextrose, and unexpected interruption of enteral feedings or parenteral nutrition. Altered consciousness from anesthesia may also alter typical hypoglycemic symptoms.

Despite the preventable nature of many inpatient episodes of hypoglycemia, institutions are more likely to have nursing protocols for the treatment of hypoglycemia than for its prevention.

5. Diabetes care providers

Diabetes management may be effectively offered by primary care physicians or hospitalists, but involvement of appropriately trained specialists or specialty teams may reduce length of stay, improve glycemic control, and improve outcomes (224–227). In the care of diabetes, implementation of standardized order sets for scheduled and correction-dose insulin may reduce reliance on sliding-scale management. A team approach is needed to establish hospital pathways. To implement intravenous infusion of insulin for the majority of patients having prolonged NPO status, hospitals will need multidisciplinary support for using insulin infusion therapy outside of critical care units or will need to develop protocols for subcutaneous insulin therapy that achieve similar glycemic goals (228).

6. DSME

Teaching diabetes self-management to patients in hospitals is a difficult and challenging task. Patients are hospitalized because they are ill, are under increased stress related to their hospitalization and diagnosis, and are in an environment that is not conducive to learning. Ideally, people with diabetes should be taught at a time and place conducive to learning: as an outpatient in a nationally recognized

program of diabetes education classes.

For the hospitalized patient, diabetes "survival skills" education is generally considered a feasible approach. Patients are taught sufficient information to enable them to go home safely. Those newly diagnosed with diabetes or who are new to insulin and or blood glucose monitoring need to be instructed before discharge to help ensure safe care upon returning home. Those patients hospitalized because of a crisis related to diabetes management or poor care at home need education to hopefully prevent subsequent episodes of hospitalization.

7. MNT

Even though hospital diets continue to be ordered by calorie levels based on the "ADA diet," it has been recommended that the term "ADA diet" no longer be used (229). Since 1994, the ADA has not endorsed any single meal plan or specified percentages of macronutrients. Current nutrition recommendations advise individualization based on treatment goals, physiologic parameters, and medication usage.

Because of the complexity of nutrition issues, it is recommended that a registered dietitian, knowledgeable and skilled in MNT, serve as the team member who provides MNT. The dietitian is responsible for integrating information about the patient's clinical condition, eating, and lifestyle habits and for establishing treatment goals in order to determine a realistic plan for nutrition therapy (229).

8. Bedside blood glucose monitoring

Implementing intensive diabetes therapy in the hospital setting requires frequent and accurate blood glucose data. This measure is analogous to an additional "vital sign" for hospitalized patients with diabetes. Bedside glucose monitoring using capillary blood has advantages over laboratory venous glucose testing because the results can be obtained rapidly at the "point of care," where therapeutic decisions are made. For this reason, the terms bedside and point-of-care glucose monitoring are used interchangeably.

For patients who are eating, commonly recommended testing frequencies are premeal and at bedtime. For patients not eating, testing every 4–6 h is usually sufficient for determining correction insulin doses. Patients controlled with continuous intravenous insulin typically require hourly blood glucose testing until the blood glucose levels are stable, then every 2 h.

Bedside blood glucose testing is usually performed with portable glucose devices that are identical or similar to devices for home SMBG. Ability to track the occurrence of hypo- and hyperglycemia is necessary.

9. Continuous blood glucose monitoring

The introduction of real-time blood glucose monitoring as a tool for outpatient diabetes management has potential benefit for the inpatient population (230). However, at this time, data are lacking examining this new technology in the acutely ill patient population. Until more studies are published, it is premature to use continuous blood glucose monitoring except in a research setting.

Case 1:05-cv-00360-SLR Document 401-10 Filed 05/13/2008 Page 49 of 90

B. Diabetes care in the school and day care setting (184)

Recommendations

- An individualized diabetes medical management plan (DMMP) should be developed by the parent/guardian and the student's diabetes health care team. (E)
- A 504 plan should be developed and implemented by the family, school nurse, and diabetes health care team. (E)
- An adequate number of school personnel should be trained in the necessary diabetes procedures (including monitoring of blood glucose levels and administration of insulin and glucagon) and in the appropriate response to high and low blood glucose levels. These school personnel need not be health care professionals. (E)
- The student with diabetes should have immediate access to diabetes supplies at all times, with supervision as needed. (E)
- The student should be permitted to monitor his or her blood glucose level, as developmentally appropriate and determined by the family and diabetes health care team with input by the school nurse, and take appropriate action to treat hypoglycemia in the classroom or anywhere the student is in conjunction with a school activity if indicated in the student's DMMP. (E)

There are ~206,000 individuals <20 years of age with diabetes in the U.S., most of whom attend school and/or some type of day care and need knowledgeable staff to provide a safe environment. Despite legal protections, children in the school and day care setting still face discrimination. Parents and the health care team should provide school systems and day care providers with the information necessary by developing an individualized DMMP, including information necessary for children with diabetes to participate fully and safely in the school/day care experience. Appropriate diabetes care in the school and day care setting is necessary for the child's immediate safety, long-term well-being, and optimal academic performance.

An adequate number of school personnel should be trained in the necessary diabetes procedures (e.g., blood glucose monitoring and insulin and glucagon administration) and in the appropriate response to high and low blood glucose levels. This will ensure that at least one adult is present to perform these procedures in a timely manner while the student is at school, on field trips, and during extracurricular activities or other school-sponsored events. These school personnel need not be health care professionals.

Case 1:05-cv-00360-SLR Document 401-10 Filed 05/13/2008 Page 30 of 90

The student with diabetes should have immediate access to diabetes supplies at all times, with supervision as needed. A student with diabetes should be able to obtain a blood glucose level and respond to the results as quickly and conveniently as possible, minimizing the need for missing instruction in the classroom. Accordingly, a student who is capable of doing so should be permitted to monitor his or her blood glucose level and take appropriate action to treat hypoglycemia in the classroom or designated area adjacent to the classroom or anywhere the student is in conjunction with a school activity. The student's desire for privacy during testing should also be accommodated.

C. Diabetes care at diabetes camps (231)

Recommendations

- Each camper should have a standardized medical form completed by his/her family and the physician managing the diabetes. (E)
- It is imperative that the medical staff is led by someone with expertise in managing type 1 and type 2 diabetes and includes a nursing staff (including diabetes educators and diabetes clinical nurse specialists) and registered dietitians with expertise in diabetes. (E)
- All camp staff, including medical, nursing, nutrition, and volunteer, should undergo background testing to ensure appropriateness in working with children. (E)

The concept of specialized residential and day camps for children with diabetes has become widespread throughout the U.S. and many other parts of the world. The mission of camps specialized for children and youth with diabetes is to allow for a camping experience in a safe environment. An equally important goal is to enable children with diabetes to meet and share their experiences with one another while they learn to be more personally responsible for their disease. For this to occur, a skilled medical and camping staff must be available to ensure optimal safety and an integrated camping/educational experience.

The diabetes camping experience is short term and is most often associated with increased physical activity relative to that experienced while at home. Thus, goals of glycemic control are more related to the avoidance of extremes in blood glucose levels than to the optimization of intensive glycemic control while away at camp.

Each camper should have a standardized medical form completed by his/her family and the physician managing the diabetes that details the camper's past medical history, immunization record, and diabetes regimen. The home insulin dosage should be recorded for each camper, including number and timing of injections or basal and bolus dosages given by CSII and type(s) of insulin used.

During camp, a daily record of the camper's progress should be made. All blood glucose levels and insulin dosages should be recorded. To ensure safety and optimal diabetes management, multiple blood glucose determinations should be made throughout each 24-h period: before meals, at bedtime, after or during prolonged and strenuous activity, and in the middle of the night when indicated for prior hypoglycemia. If major alterations of a camper's regimen appear to be indicated, it is important to discuss this with the camper and the family in addition to the child's local physician. The record of what

DJA-1448